EXHIBIT A

MARKETING NEURONTIN

Expert Report of Charles King III

22 October 2007

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I. Summary

1. Pfizer Inc. markets and sells the prescription drug Neurontin®. In December 1993, the Food and Drug Administration (FDA) approved Neurontin only for the adjunctive treatment of partial seizures in persons with epilepsy older than 12 years of age at daily dosages up from 900 mg to 1800 mg. Parke-Davis Pharmaceuticals started selling Neurontin in January 1994. Neurontin subsequently received additional FDA approvals for use as adjunctive therapy for treatment of seizures in children (October 2000) and for the management of post-herpetic neuralgia in adults (May 2002). Pfizer acquired Warner-Lambert LLC (Warner-Lambert) and its Parke-Davis division in 2000.

2. I have been retained by counsel to address certain marketing and economic issues with respect to the off-label promotion of Neurontin.

3. It is my understanding that it is illegal for drug companies to promote drugs for other, so-called "off-label," uses that do not have FDA approval. I also understand the following. Beginning in the mid-1990s, Neurontin was heavily promoted and widely used for the off-label treatment of pain syndromes and psychiatric conditions, including bipolar disorder. In 2004, Warner-Lambert, the original developer of Neurontin, admitted guilt and settled litigation charging that during the 1990s Warner-Lambert violated federal regulations by promoting Neurontin for pain, psychiatric conditions, migraine, and other unapproved uses. Since acquiring Warner-Lambert in 2000, Pfizer has continued to promote Neurontin for these and other unapproved uses. Pfizer has failed to disclose the lack of efficacy of Neurontin for certain off-label uses, suppressed information about its serious adverse events, and made false and misleading statements about Neurontin and its unapproved uses.

4. On the basis of the above understanding of facts, counsel has retained me to provide an expert opinion with respect to four main questions:

a. Were the marketing and promotional efforts of Warner-Lambert and Pfizer significant contributing factors to the off-label sales of Neurontin?

b. Would significant off-label sales of Neurontin have continued had Pfizer ceased off-label promotional activities for Neurontin?

c. Did the suppression of information about serious adverse events enable growth in off-label sales?

d. Did Pfizer's off-label marketing of Neurontin indirectly influence all physicians prescribing of Neurontin?

5. In response to these questions, it is my opinion that:

a. The marketing and promotional efforts of Warner-Lambert and Pfizer were significant contributing factors to the off-label sales of Neurontin.

b. Off-label sales of Neurontin would have continued had Pfizer ceased off-label promotional activities for Neurontin.

c. The suppression of information about serious adverse events enabled growth in off-label sales.

d. Pfizer's off-label marketing of Neurontin indirectly influenced all, or substantially, all physicians prescribing of Neurontin.

II. Qualifications

6. I am a Special Consultant to Greylock McKinnon Associates, a consulting and litigation support firm located in Cambridge, Massachusetts. As an economist, I specialize in marketing, industrial organization, microeconomics and econometrics.

7. I have taught economics, marketing and statistical methods in economics; conducted marketing and economic research; and provided economic and marketing consulting in my areas of specialization. As an Assistant Professor in Marketing at the Harvard Business School from 1997 to 2003, I taught courses in marketing, information and network economics, and organizational economics in the Masters and Doctoral programs. I also taught in Harvard Business School's executive education program for pharmaceutical companies and in IBM's Premier Program on competitive strategy. Since 1981, I have consulted to private corporations, nonprofit corporations, law firms, consulting companies and research organizations. Since 2001, I have served as a member of the Editorial Review Board for *Journal of Public Policy & Marketing*. I have been and continue to be a research referee for a variety of academic journals and the Robert Wood Johnson Foundation. I am the author of various refereed journal articles, working papers and consulting reports.

8. My research activities include issues concerning health care and the pharmaceutical industry. For example, I have written an academic working paper[1] analyzing marketing, product differentiation and competition in the pharmaceutical drug market at issue in this case and published a case study[2] evaluating Pepcid's race against Zantac and other competitors to enter the over-the-counter market. I have published a variety of peer-reviewed articles and cases,[3] including applications of marketing and economic analyses to health care and pharmaceutical issues.

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[1] C. King, "Marketing, Product Differentiation and Competition in the Market for Antiulcer Drugs," Harvard Business School, Working Paper No. 0-014 (Sept. 2000).

[2] E.R. Berndt, C. King, L. Klein and A.J. Silk, "Pepcid AC: The Race to Enter the OTC Market," (9-500-073), Harvard Business School. Also published in *Problems and Cases in Health Care Marketing*, edited by J.T. Gourville, J.A. Quelch and V.K. Rangan, McGraw-Hill Irwin, 2003.

[3] *See* C. King and D. Narayandas, "Coca-Cola's New Vending Machine (A): Pricing To Capture Value, or Not?" (9-500-068), Harvard Business School; E.R. Berndt, C. King, L. Klein and A.J. Silk, "Pepcid AC: The Race to Enter the OTC Market," (9-500-073), Harvard Business School (also published *in Problems and Cases in Health Care Marketing*, edited by J.T. Gourville, J.A. Quelch and V.K. Rangan. McGraw-Hill Irwin, 2003).

9. I have experience in applying economic and marketing theories to the pharmaceutical industry. I have submitted testimony and consulted in litigation involving health care and pharmaceutical markets and industries including:

- Consulting in the litigation brought by the Massachusetts Attorney General against the tobacco companies. Working with a team of health care experts, I submitted written testimony assessing and measuring the impacts of smoking on Medicaid health costs in The Commonwealth of Massachusetts.[4]

- Serving as an expert witness for the plaintiffs in *Daniels v. Philip Morris Cos*.[5] In that assignment I examined the magazine advertising patterns of cigarette manufacturers.

- Testifying before the United States Senate on the effect of the Master Settlement Agreement on the potential exposure of young people to cigarette advertising in magazines.[6]

- Testifying on the issues of liability and market definition in an antitrust case involving the prescription drug Relafen.[7]

- Submitting written testimony regarding discovery and class certification and consulting to counsel for the plaintiffs regarding damages in a case involving the prescription drugs Celebrex and Vioxx.[8]

- Submitting written testimony analyzing impact and class certification and consulting to counsel for the plaintiffs regarding damages for the class of direct purchasers of the anti-depressant Paxil[9] and for the class of

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[4] The results of this work are described in D. Cutler, A. Epstein, R. Frank, R. Hartman, C. King, J. Newhouse, E. Richardson and M. Rosenthal, "How Good a Deal was the Tobacco Settlement?: Assessing Payments to Massachusetts," *Journal of Risk and Uncertainty* (2000), 21 (2/3).

[5] *Daniels v. Philip Morris Cos.*, 18 F. Supp. 2d 1110 (Southern District of California, 1998).

[6] C. King, Statement Before the Committee on Governmental Affairs, Subcommittee on Oversight of Government Management, Restructuring and the District of Columbia, United States Senate, May 14, 2002 (available at <http://hsgac.senate.gov/051302king.pdf> as accessed October 2007).

[7] *In re Relafen Antitrust Litigation*, United States District Court, D. Mass. Master File No. 01-CV-12222-WGY.

[8] *Heindel et al. v. Pfizer et al.* (hereafter *Heindel*), United States District Court, D. New Jersey, Civil Action, Case No. 02-3348 (GEB).

[9] *The Stop & Shop Supermarket Company et al. v. SmithKline Beecham Corporation*, United States District Court, Eastern District of Pennsylvania, C.A. No. 03-4578.

individual purchasers of the prescription drug Vioxx in two separate cases.[10]

- Submitting written testimony on behalf of Teva Pharmaceuticals USA, Inc., as defendant, determining whether Abbott Laboratories would suffer immediate "irreparable" harm unless granted an injunction.[11]

- Submitting written testimony concerning issues pertaining to class certification, liability and product market definition, and damages and consulting to counsel for the plaintiffs for the class of end payors of the prescription drug TriCor.[12]

- Consulting to Greylock McKinnon Associates on litigation involving a broad range of markets, including agricultural, financial[13] and pharmaceutical[14] markets, and legal issues. This consulting related to the following additional drug products: Augmentin,[15] Cipro,[16] K-Dur,[17] Lipitor,[18] Lupron,[19] Neurontin,[20] Relefan[21] and Remeron.[22]

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[10] *Kleinman et al. v. Merck & Co., Inc.*, Superior Court of New Jersey Law Division: Camden County, Docket No. ATL-L-7894-04-MT and *Anderson et al. v. Merck & Co., Inc.*, Superior Court of the State of California, County Of Los Angeles, Central Civil West, Case No. BC 324384.

[11] *Abbott Laboratories v. Teva Pharmaceuticals USA Inc.*, United States District Court for the Northern District of Illinois, Eastern Division, C.A. No. 07 C 2213.

[12] *In re: TriCor Indirect Purchaser Litigation*, United States District Court, District of Deleware, C.A. No. 05-360.

[13] *Lynne A. Carnegie v. Household International, Inc., Household Bank, f.s.b., successor in interest to Beneficial National Bank, Household Tax Masters Inc., formerly known as Beneficial Tax Masters, Inc., Beneficial Franchise Company, Inc., H&R Block, Inc., H&R Block Services, Inc., H&R Block Tax Services, Inc., H&R Block Eastern Tax Services, Inc., Block Financial Corp. and HRB Royalty, Inc.*, No. 98 C 2178, United States District Court for the Northern District of Illinois Eastern Division.

[14] *In re Pharmaceutical Industry Average Wholesale Price Litigation,* United States District Court for the District of Massachusetts, MDL, No. 1456, CIVIL ACTION: 01-CV-12257-PBS.

[15] *In re Augmentin Antitrust Litigation*, United States District Court for the Eastern District of Virginia, No. 02-CV-442.

[16] *In re Ciprofloxacin Hydrochloride Antitrust Litigation*, Master File No. 1:00-MD-1383, United States District Court for the Eastern District of New York.

[17] *In re K-Dur Antitrust Litigation*, Civil Action No. 01-1652 (JAG), (Consolidated Cases), MDL No. 1419, United States District Court for the District of New Jersey.

[18] *In re American Federation of State, County and Municipal Employees, et al., Plaintiffs, vs. GlaxoSmithKline plc, and SmithKline Beecham Corporation, Defendants*, Docket No. 2:02cv442, United States District Court Eastern District of Virginia Norfolk Division.

10. I received a bachelor's degree in astronomy (*magna cum laude*) from Harvard University in 1974. I received a *juris doctor* degree in law from the Yale Law School in 1979 and a Ph.D. in economics from M.I.T. in 1997. Details of my professional experience, publications, and past testimony are described in my *curriculum vitae*, a copy of which is attached to this report as Exhibit A.

11. Greylock McKinnon Associates Inc. bills my time on this matter at an hourly rate of $475.

III. Assignment

A. Introduction

12. Pfizer Inc. markets and sells the prescription drug Neurontin. The active pharmaceutical ingredient in Neurontin is known as gabapentin. In December 1993, the Food and Drug Administration (FDA) approved Neurontin only for the adjunctive treatment of partial seizures in persons with epilepsy older than 12 years of age at daily dosages up from 900 mg to 1800 mg.[23] This meant that Neurontin was approved only as a "second-line" or add on treatment for use in conjunction with another "front-line" epilepsy drug. Parke-Davis started selling Neurontin in January 1994. Neurontin subsequently received additional FDA approvals for use as adjunctive therapy for treatment of seizures in children

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[19] *In re Lupron Marketing and Sales Practices Litigation*, United States District Court, District of Massachusetts, MDL No. 1430, CA No. 01-CV-10861.

[20] *In re Neurontin Marketing and Sales Practices Litigation*, MDL Docket No. 1629, Master File No. 04-10981, United States District Court, District of Massachusetts.

[21] *In re Relafen Antitrust Litigation,* United States District Court, District of Massachusetts, Master File No. 01-CV-12222-WGY.

[22] *In re Remeron End-Payer Antitrust Litigation*, United States District Court for the District of New Jersey, Master Docket No. 02-CV-2007.

[23] "Prior to seeking approval of the drug from the FDA, Warner-Lambert's Parke-Davis division filed a patent application on November 23, 1990, in which the company sought protection for the use of the drug has a method of treating neuro- degenerative diseases. … The [New Drug Application] submitted to the FDA sought approval on a much narrower basis that was presented the patent application." Sentencing Memorandum of the United States, Page 12. Warner-Lambert subsequently applied for and received a patent for "a novel therapeutic use of gabapentin for the treatment of mania in all its various forms," including treatment of bipolar disorder, on May 15, 1995. Pfizer APande 0000544-48.

(October 2000) and for the management of post-herpetic neuralgia[24] in adults (May 2002).[25] Pfizer acquired Warner-Lambert LLC (Warner-Lambert) and its Parke-Davis division in 2000.[26]

13. It is illegal for drug companies promote drugs for other, so-called "off-label," uses that do not have FDA approval. Beginning in the mid-1990s, Neurontin was heavily promoted and widely used for the off-label treatment of pain syndromes and psychiatric conditions, including bipolar disorder.[27] In 2004, Warner-Lambert, the original developer of Neurontin, admitted guilt and settled litigation charging that during the 1990s Warner-Lambert violated federal regulations by promoting Neurontin for pain, psychiatric conditions, migraine, and other unapproved uses.[28] Since 2000 when Pfizer acquired Warner-Lambert and Neurontin, off-label uses continue to dominate Neurontin sales.

B. Scope of the Assignment

14. Counsel has asked me to address four main questions:

a. whether the marketing and promotional efforts of Warner-Lambert and Pfizer were significant contributing factors in the off-label sales of Neurontin,

b. whether significant off-label sales of Neurontin would have continued had Pfizer ceased off-label promotional activities for Neurontin,

c. whether the suppression of information about serious adverse events enabled the growth in off-label sales, and

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[24] "Postherpetic neuralgia is a painful condition affecting your nerve fibers and skin. It's a complication of shingles, a second outbreak of the varicella-zoster virus, which initially causes chickenpox." Mayo Clinic, http://www.mayoclinic.com/health/postherpetic-neuralgia/DS00277.

[25] See, for example, Approval Letter, Center for Drug Evaluation and Research,

http://www.fda.gov/cder/foi/nda/2002/21-397.pdf_Neurontin_Approv.pdf, as accessed October 2007.

[26] In the following, references to Warner-Lambert include its Parke-Davis subsidiaryand references to Pfizer include Warner-Lambert following its purchase by Pfizer in 2000.

[27] Sentencing Memorandum, page 10.

[28] US Department of Justice. Warner-Lambert to pay $430 million to resolve criminal & civil health-care liability relating to off-label promotion. *See* "Warner-Lambert to Pay $430 Million to Resolve Criminal & Civil Health Care Liability Relating to Off-Label Promotion," available at http://www.usdoj.gov/opa/pr/2004/May/04_civ_322.htm, accessed October 14, 2007.

d. whether Pfizer's off-label marketing of Neurontin indirectly influenced all prescribing physicians of Neurontin.

C. Materials Relied Upon

15. In reaching my conclusions, I have relied upon the materials identified in Attachment B and throughout this report. I have also reviewed the results of analyses performed by Keith Altman, Finkelstein & Partners, LLP, and carried out under my direction of data requested from counsel.[29] My opinions are also based on my experience as an academic researcher in the pharmaceutical industry and my expertise as an economist specializing in marketing and industrial organization. I reserve the right to supplement my analyses and opinions in light of additional documents, data, expert reports, or testimony that may subsequently become available. I also reserve the right to prepare and use visual aids in connection with my testimony at trial.

IV. The Success of the Neurontin Off-Label Strategy

A. Growth in Neurontin Off-Label Prescriptions

16. Warner-Lambert estimated that the "ultimate" sales potential for Neurontin over the life of its patent was only $500 million because of the limited adjunctive use for which it had been approved.[30] To expand the market for Neurontin, Warner-Lambert developed a "publication strategy."[31] Its goal was "to disseminate the information [about Neurontin's potential use for psychiatric disorders, including bipolar and mood and anxiety disorders] as widely as possible through the world's medical literature"[32] as a means of generating excitement in the market and stimulating off-label prescriptions despite the lack of FDA approval.[33] Warner-Lambert calculated that this strategy would avoid

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[29] Data requested from plaintiffs council. Data computations performed by Keith Altman, Finkelstein & Partners, LLP,under my direction.

[30] See Memorandum from Walker to Laesecke, Pierce and Ulrich, 5/18/94, V090268.

[31] For an overview of the public education strategy, see generally Sentencing Memorandum of the United States and Steinman et al. article.

[32] *United States ex rel. Franklin v. Parke-Davis*, 147 F. Supp.2d 39 (D. Mass. 2001), Exhibit 171. [Inner office memorandum from Atul Pande to John Boris, re: "Gabapentin Approvals", and handwritten response]; 28 March 1995: X029227.

[33] *United States ex rel. Franklin v. Parke-Davis*, 147 F. Supp.2d 39 (D. Mass. 2001), Exhibit 26. Marketing Assessments – Neurontin in Neuropathic Pain and Spasticity [and cover letter]; 24 July 1995: WL 07520 – 07547 and Exhibit 31 [Parke-Davis memo from John Boris to "Distribution," re: "Marketing Assessments – Neurontin in Migraine," and cover letter]; 31 July 1996: V 082736 – 082761.

the costly and time-consuming clinical trials required for FDA approval.[34] Warner-Lambert, and later Pfizer, were aware that although other anticonvulsant drugs were approved for similar psychiatric applications, Neurontin worked through a different mechanism of action and that they lacked sufficient scientific evidence of Neurontin's efficacy to obtain FDA approval for these uses.[35]

17. In the years following Neurontin's initial approval, Warner-Lambert and Pfizer implemented similar strategies to promote off-label uses of Neurontin at doses of more than 1800 mg per day and for neuropathic pain, epilepsy monotherapy,[36] migraine prophylaxis, Restless Leg Syndrome (RLS)/Periodic Limb Movement Disorder (PLMD), and nociceptive[37] and non-neuropathic pain. In each case, off-label Neurontin prescriptions sharply increased after the commencement of an off-label marketing campaign, as shown in the following graphs. Although Neurontin was approved only for a specific epilepsy indication, Warner-Lambert promoted Neurontin for pain; psychiatric conditions, such as bipolar disorder and anxiety; and other unapproved uses "from at least June of 1995 through the least April of 2000, across United States."[38] Promotion of Neurontin for off-label uses continued and Neurontin prescriptions for unapproved uses increased after Pfizer acquired Warner-Lambert, as shown in Figures 1 through 6.

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[34] Parke-Davis lacked time to do proper clinical trials in support of an application to the FDA for the approval of Neurontin for other uses, because the patent was due to expire in 1998 (later extended to 2000). See, e.g., Memorandum from Mi Dong to Neurontin Anticonvulsant Development Team of 3/16/95, X028957-62 at p. X028961; Memorandum from J. Pieroni to Anton, Brandner, Cadre, Evans, Gemelli, Montgomery, and Summers of 3/22/95, V086787-91 at V086789; Interoffice Memorandum from Pande to Boris of 3/23/95, X029226; Cover letter from Brandicourt to Development Team of 7/31/95 with attached Marketing Assessments: Neurontin in Neuropathic Pain and Spasticity of 7/24/95, WL 07520-47 at WL 07524; Memorandum from Boris to NPC Committee, Development Team, and Marketing Council of 7/31/96, V082736-61 at V082737; and Memorandum from Francie Kivel to J. Boris, O. Brandicourt, E. Guerrero, J. Knoop, L. Magnus-Miller, and L. Perlow, October 26, 1995, V053848-77 at V053853.

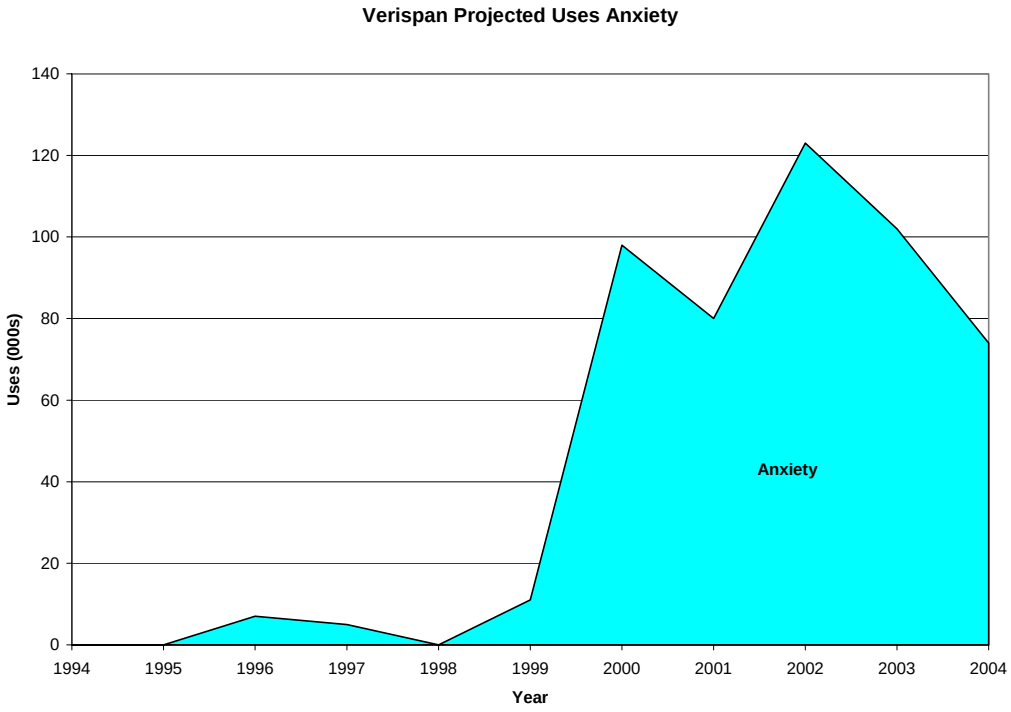
[35] "Though no preclinical data support the efficacy of gabapentin in acute mania the observations of other anticonvulsants suggests that gabapentin may be effective in the treatment of acute mania and in the prophylaxis of bipolar disorder." Pfizer_JMarino_0001272.

[36] Monotherapy refers to the use of Neurontin by itself, rather than in combination with another drug, to control epileptic seizures. Parke-Davis formally applied to the FDA for a monotherapy indication in 1996. The FDA rejected the application on the grounds at Parke-Davis had failed to demonstrate efficacy. Sentencing Memorandum of the United States, p. 24.

[37] Nociceptive pain refers to pain caused by an injury to bodily tissues.

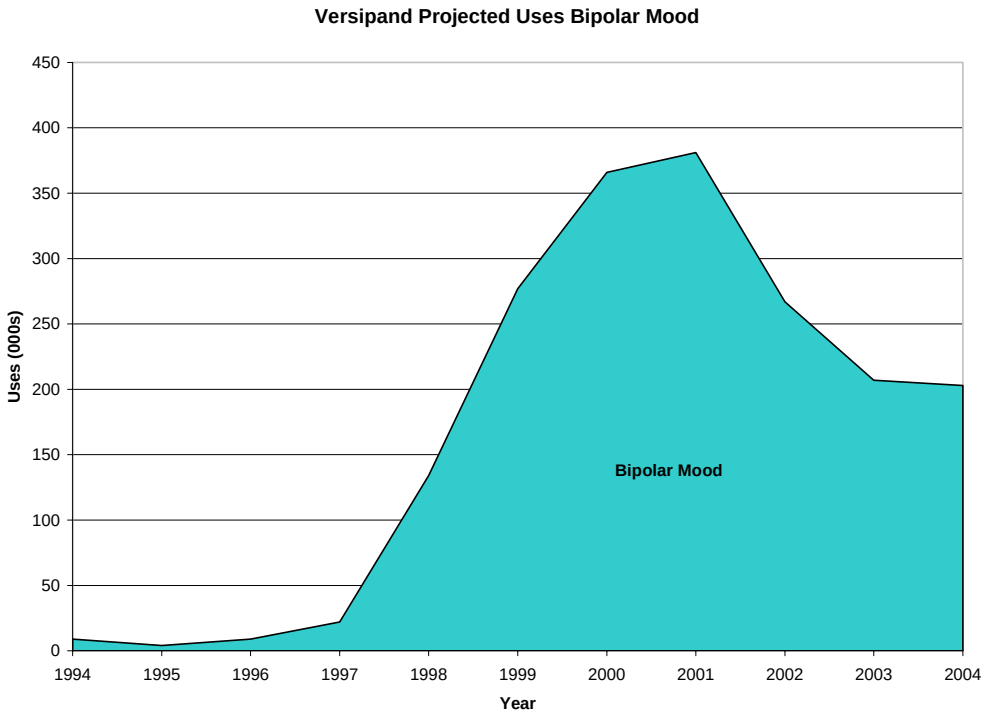
[38] Sentencing Memorandum of the United States, p. 10.

Figure 1: Off-Label Uses of Neurontin: Anxiety Disorder



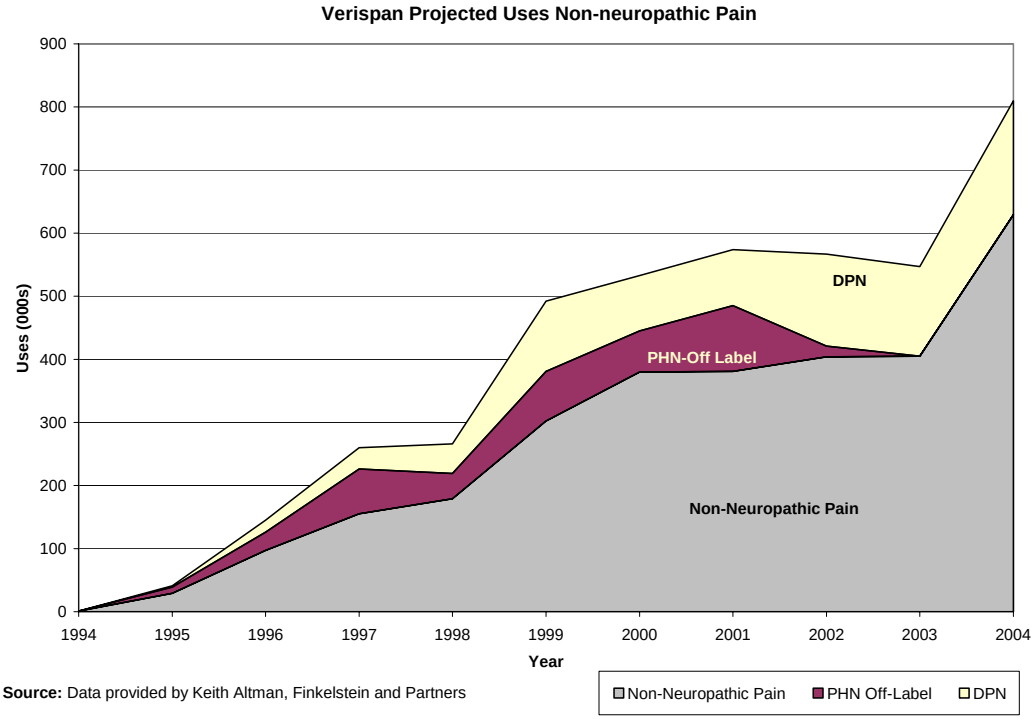
Source: Data provided by Keith Altman, Finkelstein and Partners

Figure 2: Off-Label Uses of Neurontin: Bipolar and Mood Disorders



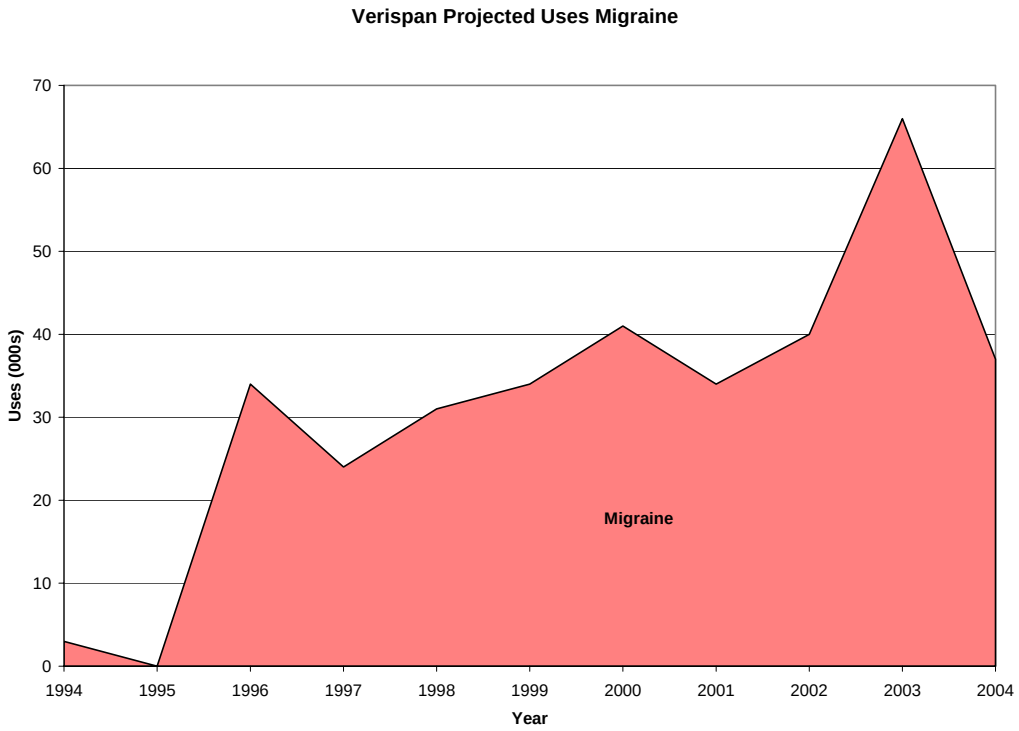
Source: Data provided by Keith Altman, Finkelstein and Partners

Figure 3: Off-Label Uses of Neurontin: Pain



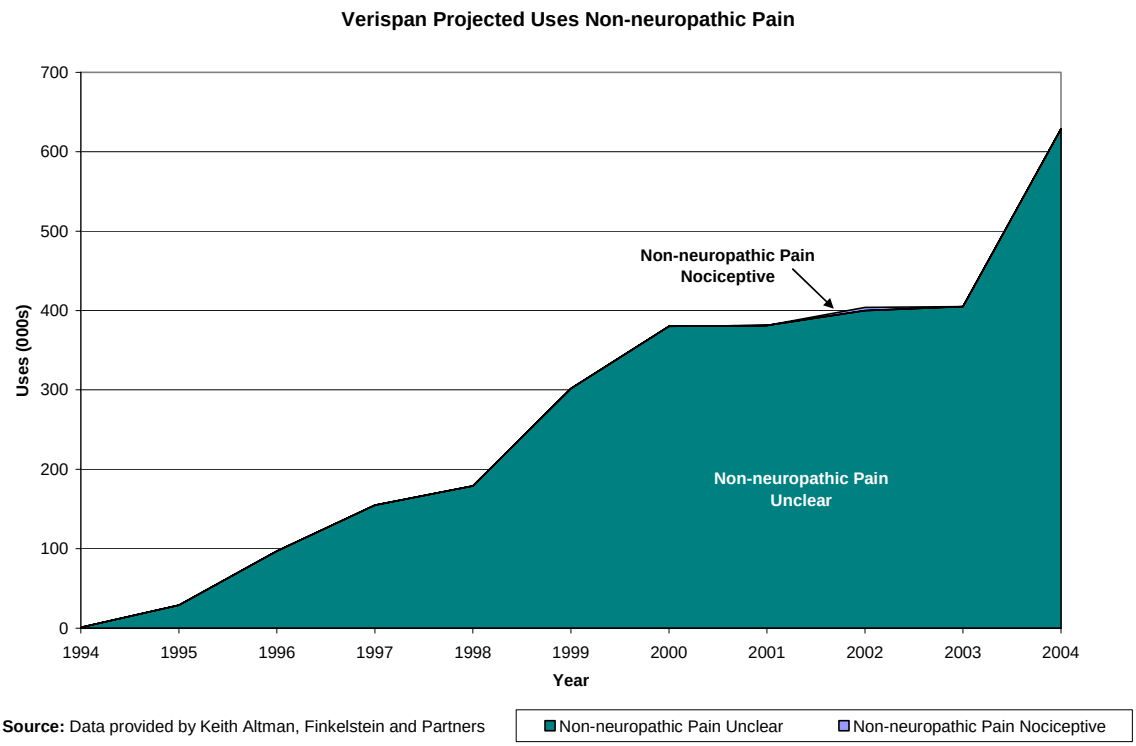
Source: Data provided by Keith Altman, Finkelstein and Partners

Figure 4: Off-Label Uses of Neurontin: Migraine and Headache



Source: Data provided by Keith Altman, Finkelstein and Partners

Figure 5: Off-Label Uses of Neurontin: Non-Neuropathic Pain



18. An unusually high percentage of Neurontin sales derived from its off-label uses.[39] In 2006, Radley et al.[40] conducted a study analyzing the off-label prescriptions of the 160 most commonly prescribed drugs.[41] The researchers found that gabapentin "had the highest portion of offlabel prescriptions"[42] of all the 160 drugs in the sample, with 83% of prescriptions being written for off-label indications. [43] The study found that in general a high proportion of all off-label drug usage lacked any clinical support, and that "[this] is especially true for

[39] Pfizer acknowledged Neurontin's high level of off-label sales was unusual: "Neurontin is the extreme example, with less than 10% of use for epilepsy, and the largest off-label use for pain management." Pfizer_CTaylor_0000414. One managed Medicaid plan found that "95% [of patients] received gabapentin for off-label diagnoses." Hamer et al., "Gabapentin use in a managed medicaid population", *Journal of Managed Care Pharmacy*, Vol. 8, No. 4, 2002, pp. 266-71.

[40] D.C. Radley, S. N. Finkelstien and S. Stafford, "Off-label Prescribing Among Office-Based Physicians", *Arch Intern Med.* , Vol. 166, May 8, 2006, pp. 1021-1026.

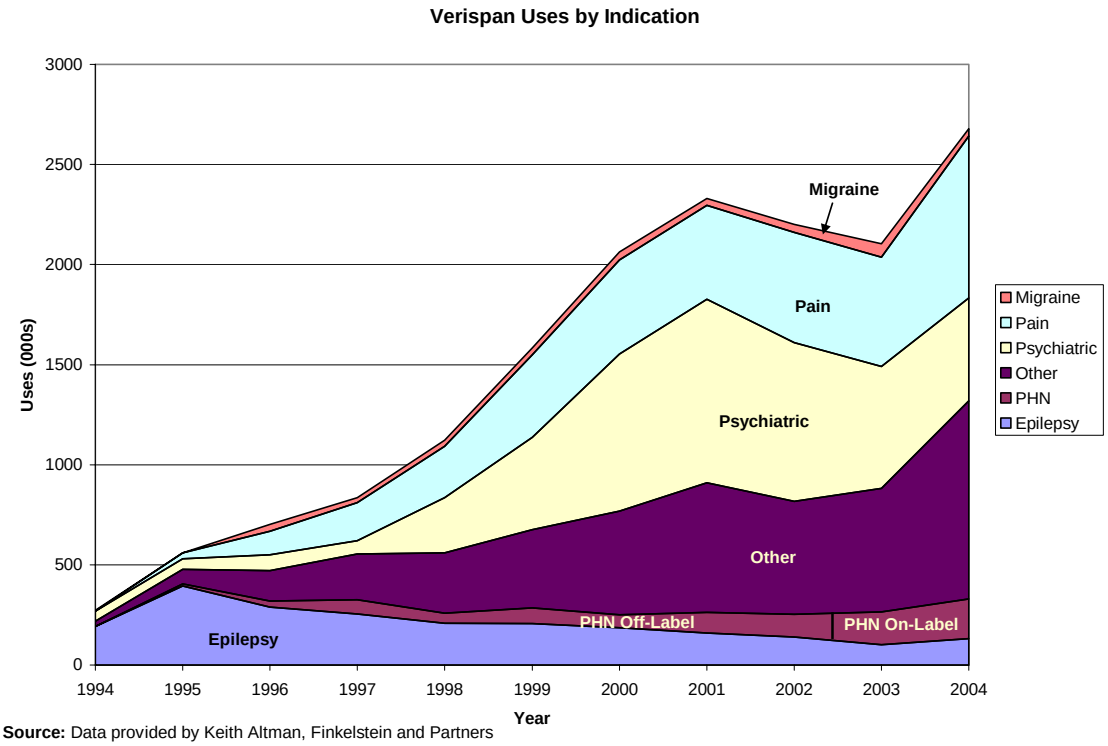
[41] Radley et al. (2006) used 2001 IMS Health National Disease and Therapeutic Index (NDTI) data in their study. In 2001, Neurontin was still under patent protection, therefore, it would have been the only source of gabapentin available to physicians, and all of the off-label prescriptions for gabapentin would essentially be off-label prescriptions for Neurontin.

[42] *Ibid*, p.1023.

[43] *Ibid*, p.1023.

gabapentin, where only 20% of its offlabel use had strong support compared with 80% with limited or no support."[44]

Figure 6: On-Label and Off-Label Uses of Neurontin



Source: Data provided by Keith Altman, Finkelstein and Partners

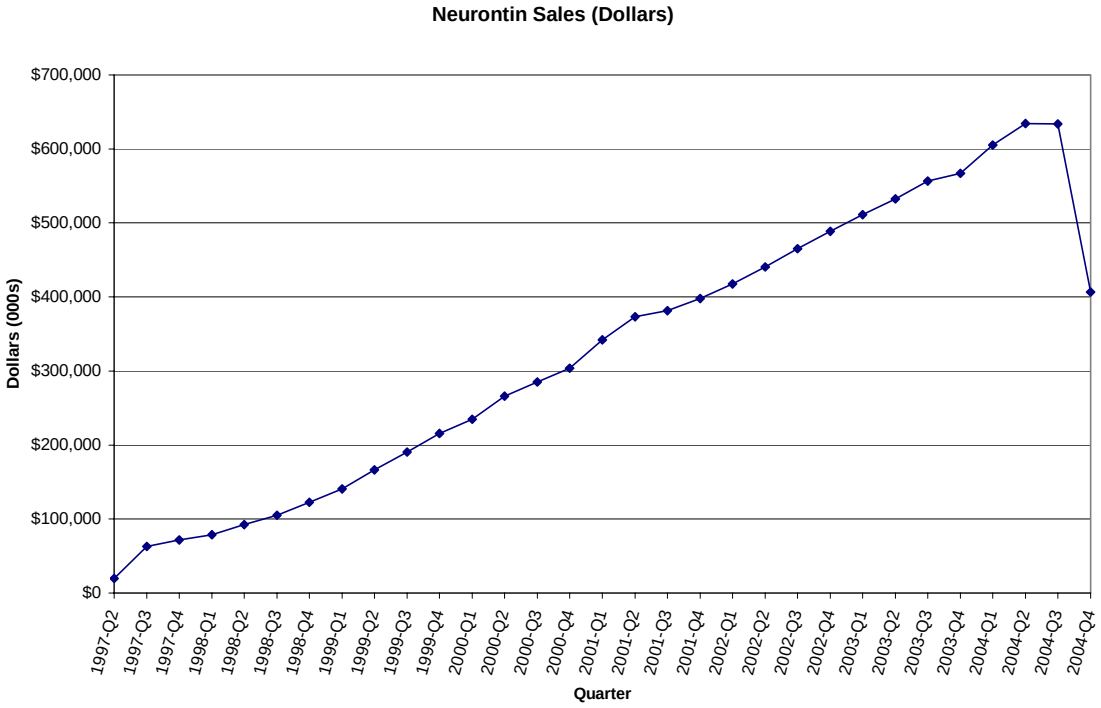
B. Growth in Neurontin Sales

19. Although Parke-Davis had predicted that Neurontin had an "ultimate" sales potential of $500 million over the life of its patent[45], Neurontin sales quickly passed this estimate. By 1999, only five years after its launch, Neurontin annual sales had already surpassed $500 million. By 2003, under Pfizer's ownership, annual sales of Neurontin were $2.4 billion.

[44] *Ibid*, pp. 1023-4. See also Affidavit of C. Seth Landefeld, M.D., and Michael Steinman, M.D., dated May 19, 2003, from Franklin case.

[45] See Memorandum from Walker to Laesecke, Pierce and Ulrich, 5/18/94, V090268.

Figure 7: Total Annual Neurontin Sales



Source: Data provided by Keith Altman, Finkelstein and Partners

V. Marketing in the Pharmaceutical Industry

20. Drug marketing is pervasive and permeates the medical profession. Most marketing efforts are targeted at influencing doctors, since they are the ones who write prescriptions. The goal is to influence doctors' prescribing habits to increase drug company profits.

21. To promote their products, drug companies spend a high percentage of their revenues on marketing. Pharmaceutical firms typically spend as much, or more, on marketing than they do on research and development.[46] Both Warner-

[46] Marcia Angell, *The Truth About the Drug Companies How They Deceive Us and What to do about it*, Random House Press, 2004.

Lambert and Pfizer spent more on promoting their drugs than they did on research and development.[47]

22. Prescription drugs are not like ordinary consumer goods. People depend on them for their health and, in some cases, even their life. Unlike typical consumer goods, prescription drugs can only be purchased under the supervision of a physician. Although patient preferences play a role, doctors exercise primary influence over health-care decisions, particularly for serious medical conditions. Doctors, as learned intermediaries, select the best drug for the patient. Since doctors ultimately decide which drugs to prescribe, pharmaceutical companies concentrate their marketing efforts on them.

A. The Drug Approval Process

Marketing expenses typically exceed research and development expenditures in the pharmaceutical industry. (See, e.g., Families USA Foundation, "Off the Charts: Pay, Profits and Spending by Drug Companies," Families USA Publication No. 01-104, July 2001, p. 1; M.A. Hurwitz and R.E. Caves, "Persuasion or Information? Promotion and the Shares of Brand Name and Generic Pharmaceuticals," *Journal of Law and Economics*, Vol. 31(2), Oct. 1988, p. 302; J. Sutton, *Technology and Market Structure*, Cambridge: The MIT Press, 1998, pp. 219-220 and footnote 17; Schweitzer, op. cit. From 1992 to 1994, the three largest U.S. pharmaceutical manufacturers – Merck, Pfizer and Eli Lilly – spent between 11% and 15% of their annual sales on research and development compared to 21% to 41% of their annual sales on marketing and promotional expenses, according to one academic study. (Schweitzer, op. cit., p. 43.)

Pharmaceutical firms spend an uncommonly large percentage of their revenues promoting their products. Promotion-to-sales ratios for prescription drugs typically range from 10 to 30 percent or more of sales, making them among the most heavily promoted of all manufactured goods. (See, e.g., K. Leffler, "Persuasion or Information? The Economics of Prescription Drug Advertising," *The Journal of Law and Economics*, Vol. 24, April 1981, pp. 45-74.) This stands in sharp contrast to advertising in the median manufacturing industry, which devotes less than 1 percent of its sales revenues to advertising. (F.M. Scherer and D. Ross, *Industrial Market Structure and Economic Performance*, Third Edition, Boston: Houghton Mifflin Company, 1990, p. 573.)

The high marketing-to-sales ratios observed in the pharmaceutical industry can be explained in terms of the underlying industry economics. Marginal production costs, the additional costs of producing one more unit of output, are typically small for pharmaceuticals. An additional dollar in sales consequently results in nearly an additional dollar in profits. Pharmaceutical companies therefore have strong incentives to increase the demand for their products. (E.R. Berndt et al., "Information, Marketing, and Pricing and the U.S. Antiulcer Drug Market," *American Economic Review*, Volume 85(2), 1995, Papers and Proceedings of the 107th Annual Meeting of the American Economic Association, Washington D.C., pp. 100-5.)

[47] Warner-Lambert's selling, distribution and administration expenses represented between 46.1 percent and 46.9 percent of its total revenues between 1998 and 2000, when it was acquired by Pfizer. During the same period, Warner-Lambert spent between 8.9 percent and 9.7 percent on research and development. Pfizer also spends more on marketing than research. From 2000 to 2006, Pfizer's selling, distribution and administrative expenses ranged between 32.2 percent and 41.1 percent of its total revenues compared to expenditures varying between 14.4 percent and 17.1 percent on research and development.

23. By law, before a new drug can be marketed, it must be approved by the Food and Drug Administration. Drugs must meet efficacy and safety standards before they can be sold. The pharmaceutical company must prove to the FDA that the drug is reasonably safe and effective for a specific use or indication. That proof typically requires a series of clinical trials to evaluate the safety and efficacy of the drug among a group of patients and nearly always includes a comparison group who do not receive the drug.

24. Drug companies generally do not conduct their own clinical trials but rely on doctors in teaching hospitals and private practice to do the studies, using either their own patients or volunteers recruited through solicitation. In the past, medical schools and teaching hospitals conducted most clinical trials. Pharmaceutical companies would provide research grants to physicians on their faculties to carry out clinical trials under institutional supervision. More recently, private companies have sprung up in the pharmaceutical industry with the sole purpose of organizing and administering drug trials. These contract research organizations (CROs) assemble and supervise groups of doctors who are paid to administer the study drugs and collect data on their effects. To obtain human subjects for clinical trials, drug companies or contract research organizations routinely pay doctors money on a per patient basis.

25. After clinical trials are completed, the drug company must file a new drug application (NDA) with the FDA to obtain approval to market the new drug. The agency and its advisory committees of outside experts review the application, the outcomes of the clinical trials, and other evidence provided by the drug company in support of its application. Only after the FDA approves the drug is it allowed on the market.

B. FDA Approves Drugs Only for Specific Uses

26. By law, drug companies are permitted to market and promote drugs only for approved uses. The FDA approves new drugs only for the specific uses, or indications, and the doses spelled out in the label or package insert that accompanies the drug. This prevents drug companies for marketing drugs for other uses, not approved by the FDA, without clinical data demonstrating the safety and efficacy of the drug for that use. It is illegal for drug companies to promote drugs for these "off-label" uses, although doctors may prescribe drugs for any use at any dosage they consider appropriate. In addition to reviewing drug labeling for accuracy, the FDA is empowered to check advertisements and promotional materials for accuracy and balance.

C. FDA Regulates Drug Promotion

27. Under the Federal Food, Drug, and Cosmetic Act and related regulations, the FDA regulates the promotion of prescription drugs.[48] Promotional materials may only make claims are supported by strict scientific evidence, and they may not be false or misleading. To ensure that doctors and consumers understand both the benefits and limitations of a drug, FDA regulations call for "fair balance" in all marketing claims and materials. The drug's risks as well as its benefits must be clearly identified, and the risks must be given appropriate prominence. All promotional materials must also be consistent with the FDA-approved product labeling. Drugs may only be marketed and promoted for their approved uses.

D. Where Doctors Get Their Information About Drugs

28. Given the pace of technological innovation and new treatments in modern medicine, physicians must keep abreast of a continuous stream of new medical developments. Doctors might be able to keep up by assiduously studying the latest medical journals and textbooks, but most do not have the time[49]. Where then do doctors get their information on which drugs to prescribe for their patients? Physicians rely upon the published medical literature as "the ultimate basis for most treatment decisions."[50] "[P]hysicians prefer to obtain information from journals and books, but also … they often consult colleagues to get answers to clinical and research questions."[51] Most depend, at least in part, on the scientific integrity of the medical process to provide them with unbiased sources of information. They scour medical journals for the latest research. They participate in conferences, meetings, and continuing medical education (CME) events to learn from experts and "opinion leaders" in the field.[52] They consult

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[48] Federal regulations for prescription drug advertising are outlined in 21 CFR 202.1.

[49] Continuing education meeting polls found "most physicians spend less than an hour a week reading." J. M. Grimshaw et al., "Changing physicians' behavior: What works and thoughts on getting more things to work", *Journal of Continuing Education in the Health Professions*, Vol. 22, 2002, pp.237-43.

[50] F. Davidoff, C.D. DeAngelis, J.M. Drazen, M.G. Nicholls, J. Hoey, L. Hojgaard, *et al*. "Sponsorship, Authorship, and Accountability," *The New England Journal of Medicine*, Volume 345(11), September 2001, 825-82 and *The Journal of the American Medical Association*, Volume 286(10), September 2001, 1232-1234. An editorial in *The American Journal of Psychiatry* notes: "[s]urveys of physicians find that over 90% of us look to original articles in medical journals as our most preferred source of new information for help in treating patients." (D.A. Lewis, R. Michels, D.S. Pine, S.K. Schultz, C.A. Tamminga, R. Freedman, "Conflict of Interest," *The American Journal of Psychiatry*, Volume 163(4), April 2006, 571-3.)

[51] Haug,James, "Physicians' preferences for information sources: a meta-analytic study", *Bull Medical Library Association*, Vol.85, July 1997.

[52] Within the medical community there is a hierarchy of influence. The opinion of medical specialists, for example, generally carries more weight within the profession than those of general practitioners.

textbooks and medical references for expert recommendations on best practice derived from the body of scientific evidence.

29. As a practical matter, doctors are constrained in their abilities to absorb the continuous stream of information about new treatments by their limited time and cognitive abilities.[53] Doctors are often not aware of the latest scientific evidence on treatments and rely heavily on information provided by drug companies in marketing and promoting their products.[54] Marketing's role in informing physicians has been widely studied over the years.[55] A recent study of the United States market for antiulcer drugs found that marketing had more of an impact on demand than clinical research.[56]

E. Marketing Drugs

30. Drug companies employ six primary marketing tools to promote their products to physicians and consumers: personal selling (or "detailing"), direct mail, medical journal advertising, free samples to physicians, medical education events and direct-to-consumer advertising. Drug sales representatives are ubiquitous in the medical world.[57] Drug company sales representatives visit doctors in their offices and hospitals to promote their products. Drug company sales representatives have traditionally played a role in informing doctors about

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[53] F.M. Scherer, "The Pharmaceutical Industry" in eds. A.J. Culyer and J.P. Newhouse, *Handbook of Health Economics*, Elsevier, 2000, pp. 1300-1302.

[54] See, e.g., S. Schweitzer, *Pharmaceutical Economics and Policy*, New York: Oxford University Press, 1997, p. 43. From E.R. Berndt, "The U.S. Pharmaceutical Industry: Why a Major Growth in Times of Cost Containment?" *Health Affairs*, Vol. 20(2) 2001, pp. 111-2:

> Marketing provides technology-transfer information to patients and providers on efficacy in the treatment of specific medical disorders based on clinical trial data; the incidence of side effects, adverse interactions, and contraindications; pharmacokinetic properties involving half-life and dosage; and, in the naturalistic environment outside the clinical trial setting, effectiveness information on post-launch product surveillance evidence, actual dosages, off-label usage (when appropriate), subpopulation differentials, tolerability, and cost effectiveness.

[55] See, *e.g.*, Schweitzer's discussion of academic and marketing studies, Schweitzer, *op. cit.*, p. 46.

[56] P. Azoulay, "Do Pharmaceutical Sales Respond to Scientific Evidence?" *Journal of Economics & Management Strategy*, Volume 11, No. 4, Winter 2002, pp. 551-594.

[57] Currently, there approximately 100,000 pharmaceutical sales representatives in the United States. M. Adams, "Drug reps use psychological tactics to successfully influence doctors' prescribing habits", *News Target Network*, July 30, 2007, http://www.newstarget.com/021956.html, accessed September 21, 2007.

the new medicines, products and therapies;[58] providing free drug samples; answering physicians' questions and maintaining goodwill. The distribution of free drug samples ("sampling") also targets doctors directly. Sampling is designed to increase sales by building a physician's personal experience with the drug and increasing his or her confidence in prescribing it.[59] Medical education events, such as symposia, conferences, and lectures, have a substantial influence on prescribing behavior.[60] Pharmaceutical companies subsidize and sponsor these programs as one component of their overall promotion strategy.[61]

F. Marketing Neurontin for Off-Label Uses

31. Since the drug company educates the medical profession and the public about its drugs and the conditions they treat, this creates an inherent conflict of interest between selling drugs and evaluating them. Most of these medical educational activities are directed towards doctors. In the case of Neurontin, it was crucial for Warner-Lambert and allegedly Pfizer to maintain that these expenditures were for education, not promotion, so that it could evade legal constraints on its marketing activities.[62] Drug company sponsorship does not mean that research is necessarily biased, but in the case of Neurontin, the drug company allegedly influenced the research, subverted the scientific process, and biased the sources that doctors relied upon for unbiased information.[63]

G. Doctors Depend on the Integrity of the Scientific Process for Unbiased Information About Drugs

32. Doctors depend on the integrity of the scientific process for accurate and reliable information about the drugs they prescribe. Warner-Lambert and Pfizer allegedly subverted the scientific process in two ways: by what they did and by what they did not do. Warner-Lambert and Pfizer allegedly promoted off-label uses of Neurontin by making false claims about its uses and efficacy. Warner-

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[58] See, e.g., D. Dogramatzis, *Pharmaceutical Marketing: A Practical Guide*, Colorado: IHS Health Group, 2002.

[59] Schweitzer, *op. cit.*, p. 49

[60] "One study of prescribing decisions by general physicians found that seminars, conferences, and lectures organized by pharmaceutical companies had more influence than advertisements, promotional material (e.g., samples, calendars, or diaries), or direct mail. Moreover, many of the doctors surveyed did not interpret such 'educational' activity as promotion (Pitt and Nel 1988)." Schweitzer, *op. cit.*, p. 52.

[61] Schweitzer, *op. cit.*, p. 52

[62] Sentencing Memorandum of the United States, pp 40-42; Steinman et al. (2006), pp. 286-288.

[63] See, e.g., Sentencing Memorandum of the United States; Steinman et al. (2006).

Lambert and Pfizer allegedly failed to disclose or omitted information about Neurontin's lack of efficacy and its side effects. Both these actions would have affected the prescribing habits of physicians.

H. How Drug Company Promotion Influences Doctors

33. The effect of drug promotion on physician beliefs, knowledge, and self-reported behavior has been widely studied.[64] Although doctors generally do perceive pharmaceutical marketing to be effective, they do not appear to recognize their own susceptibility to commercial influences.[65] Academic studies suggest that inaccurate, incorrect or misleading information about drugs may be frequently conveyed in promotional settings,[66] that doctors do not consistently distinguish between correct and incorrect information,[67] and that the perceived –

[64] See footnotes 65 - 73 and E. Clayton, "'Tis Always the Season for Giving," CALPIRG Report, September 2004; Editorial Staff, "Pharmaceutical Marketing to Physicians: Free Gifts Carry a High Price," *American Medical News*, 10 June 2002; A. Wazana, "Physicians and the Pharmaceutical Industry," *The Journal of the American Medical Association,* 283:373-380, 2000; A. Fugh-Berman, "The Corporate Coauthor," *Journal of General Internal Medicine,* 20(6):546-8, June 2005.

[65] J. Avorn, M. Chen, and R. Hartley, "Scientific Versus Commercial Sources of Influence on the Prescribing Behavior of Physicians," *American Journal of Medicine,* 73 (1), 4–8, 1982.

[66] M. Bowman and D. Pearle, "Changes in Drug Prescribing Patterns Related to Commercial Company Funding of Continuing Medical Education," *Journal of Continuing Education in the Health Professions* 8:13–20, 1988; M. G. Ziegler, P. Lew, B. C. Singer (1995) "The Accuracy of Drug Information from Star Pharmaceutical Sales Representatives," JAMA 273: 1296-1298; E. Hemminki (1997), "Content Analysis of Drug-Detailing by Pharmaceutical Representatives," Med Educ 11:210-215; D. Stryer and L.A. Bero, "Characteristics of Materials Distributed by Drug Companies. An Evaluation of Appropriateness," J. Gen Intern Med 11: 575-583; H.A. Waxman, (2005), "Memorandum to Democratic Members of House Government Reform Committee: a Marketing of Vioxx to Physicians," available: HTTP://www.democrats.reform.house.gov/documents/20050505114932-41272.pdf; E.E. Roughead, A. L. Gilbert and K.J. Harvey (1998), "Self-Regulatory Codes of Conduct: Are They Effective in Controlling Pharmaceutical Representatives' Presentations to General Medical Practitioners?" Int J Health Serv 28:269-279; J. Lexchin (1997), "What Information do Physicians Receive from Pharmaceutical Representatives?" Can Fam Physician 43: 941-945.

[67] M. G. Ziegler, P. Lew, B. C. Singer (1995) "The Accuracy of Drug Information from Star Pharmaceutical Sales Representatives," JAMA 273: 1296-1298; D. Stryer and L.A. Bero, "Characteristics of Materials Distributed by Drug Companies. An Evaluation of Appropriateness," J. Gen Intern Med 11: 575-583; A. E. Shaughnessy, D. C. Slawson and J.H. Bennett (1994), "Separating the Wheat from the Chaff: Identifying Fallacies in Pharmaceutical Promotion," J Gen Intern Med 9: 563-568; W. Molloy, D. Strand, G. Guyatt et al. (2002), "Assessing the Quality of Drug Detailing," Journal of Clinical Epidemiology 55:825-832.

rather than the actual – quality of information changes doctor behavior.[68] Doctors typically deny that gifts and payments influence their prescribing behavior.[69]

34. Research studies have investigated the association between specific types of physician behavior and free samples, contact with drug company sales representatives, attendance of company-sponsored events, and gifts. These studies have demonstrated a positive effect of drug promotion and company-sponsored continuing medical education (CME) on a) prescription of the specific drug promoted,[70] b) prescription of new drugs in place of older, generic products,[71] and c) formulary requests.[72]

35. In the case of Neurontin, drug company representatives frequently promoted unapproved uses, and their sales calls often resulted in doctors planning to increase their use Neurontin.[73]

I. How Economic Considerations Affect Drug Usage

36. Widespread insurance coverage means that doctors and their patients will be relatively insensitive to drug prices and will rationally experiment with therapies with relatively low expected benefits.[74] Doctors and their patients also face an information problem in choosing the right drug that may prevent the market from functioning efficiently.[75] Drugs, like Neurontin, are "credence goods," which means their effect may never be known because multiple factors

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[68] J. E. Calfee and D. J. Ringold (1994), "The 70% Majority: Enduring Consumer Beliefs about Advertising," Journal of Public Policy and Marketing, Volume 13, pp. 228-28; C. I. Hovland and W. Weiss (1951), "The Influence of Source Credibility on Communication Effectiveness," Public Opinion Quarterly, Volume 15, pp. 635-650.

[69] A. Wazana, op. cit., 2000; W. Sandberg et al., "The Effect of Educational Gifts from Pharmaceutical Firms on Medical Students' Recall of Company Names or Products," *Academic Medicine*, 72:916-918, 1997; B. Hodges, "Interactions with the Pharmaceutical Industry: Experiences and Attitudes of Psychiatry Residents, Interns and Clerks," *Canadian Medical Association Journal,* 1:153(5):553-9, September 1995.

[70] *Ibid.*

[71] M.Y. Peay and E.R. Peay, "The Role of Commercial Sources in the Adoption of a New Drug," *Social Science & Medicine.*, 26:1183-1189, 1988.

[72] M. Chren and C. Landefeld, "Physicians' Behavior and Their Interactions with Drug Companies: A Controlled Study of Physicians Who Requested Additions to a Hospital Drug Formulary," *The Journal of the American Medical Association*, 271, 684-689, 1994.

[73] Michael A. Steinman, G. Michael Harper, et al. (2007), "Characteristics and Impact of Drug Detailing for Gabapentin," PLoS Medicine, April 2007, Volume 4, Issue 4, pp. 0743–0751.

[74] J.P. Newhouse and the Insurance Experiment Group, *Free for All? Lessons from the RAND Health Insurance Experiment*, Cambridge: Harvard University Press, 1993.

[75] Nobel prize winning economist Kenneth Arrow first recognized this problem (K. Arrow, "Uncertainty and the Welfare Economics of Medical Care," *The American Economic Review*, 53:941-73, 1963).

can affect the course of an illness. This problem is exacerbated for Neurontin because many of the "off-label" uses of Neurontin have large "placebo effects".[76] As a result, market forces are likely to fail to protect consumers against false drug claims.

VI. Marketing Neurontin in the Warner-Lambert Era (1994 – 2000)

A. Creation of the Off-Label Strategy

37. Neurontin was initially approved only for epileptic seizures in adult patients who had failed to improve using other treatments, a limited market.[77] Yet Neurontin became a one of the world's best-selling drugs, as sales for unapproved uses grew to approximately 90 percent of sales (See Figure 8).[78] Off-label uses for Neurontin grew from approximately 15 percent of all uses in 1994 when Neurontin was first marketed to 94 percent of all uses in the United States by 2002.[79]

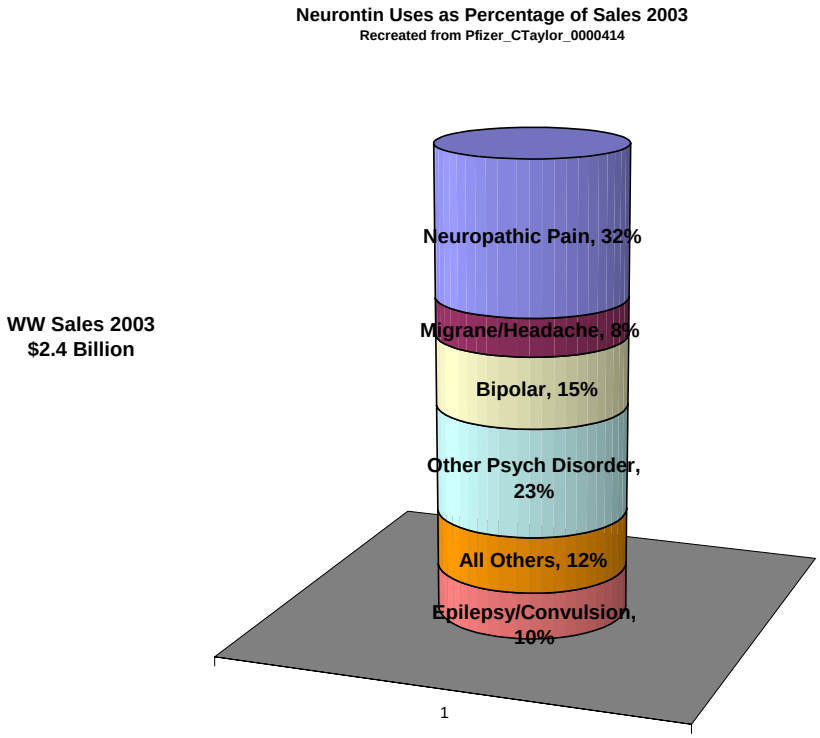
Figure 8: Neurontin Sales for Unapproved Uses Were Approximately 90 Percent of Total Sales in 2003.

[76] The placebo effect is defined as: "A remarkable phenomenon in which a placebo -- a fake treatment, an inactive substance like sugar, distilled water, or saline solution -- can sometimes improve a patient's condition simply because the person has the expectation that it will be helpful." MediceNet.com (http://www.medterms.com/script/main/art.asp?articlekey=31481) Placebo effects are widespread in clinical research and practices and have been widely studied. See, for example, Fabrizio Benedetti and Martina Amanzio, "The Neurobiology of Placebo Analgesia: From Endogenous Opiods to Cholecystokinin," *Progress in Neurology*, Vol. 51, pp. 109-125, 1997; Frederic M. Quitkin, "Placebos, Drug Effects, and Study Design: A Clinician's Guide," *American Journal of Psychiatry*, 156:6, June 1999 (placebo response rates vary from 25 to 60% for patients with major depressive disorders); Asbjorn Hrobjartsson and Peter Gotzche, "Is the Placebo Powerless? An Analysis of Clinical Trials Comparing Placebo with No Treatment," *The New England Journal of Medicine*, Vol. 344, No. 21, May 24, 2001 (review of 27 trials involving pain treatment "showed a significant effect of placebo as compared with no treatment"); Marlena A. Piercy, John J. Sramek, Neal M. Kurtz and Neal R. Cutler, "Placebo Response in Anxiety Disorders," *The Annals of Pharmacotherapy*, Vol. 30, No. 9, 1996, pp. 1013-1019 (summarizes placebo response rates: generalized anxiety, 18-67%; panic disorders, 20-134%; social phobia, 7-43%; and obsessive-compulsive disorder, 7-19%).

[77] See ¶¶ 12 and 16.

[78] In 2003, Neurontin ranked 10th in U.S. sales (Drugs.com, http://www.drugs.com/top200_2003.html) with sales of $2.4 billion.

[79] Sentencing Memorandum of the United States, p. 13.



38. Warner-Lambert promoted Neurontin for the treatment of bipolar disorder, a psychological condition, even though a study had shown that the medicine was no better than a placebo in treating the disorder.[80] Other disorders for which Neurontin was illegally promoted included various pain disorders, anxiety disorder, social phobias, amyotrophic lateral sclerosis (ALS, a degenerative nerve disease commonly referred to as Lou Gehrig's disease), attention deficit disorder, migraine, drug and alcohol withdrawal seizures, restless leg syndrome, and as a first-line monotherapy treatment for epilepsy (using Neurontin alone, rather than in addition to another drug).[81]

39. Warner-Lambert executives started exploring ways to expand the market for Neurontin beyond the scope of its initial FDA approval soon after its

[80] Pande AC, Crockatt JG, Janney CA, Werth JL, Tsaroucha G. Gabapentin in bipolar disorder: a placebo-controlled trial of adjunctive therapy. Gabapentin Bipolar Disorder Study Group. Bipolar Disord. 2000;2:249-55. [PMID:11249802].

[81] Sentencing Memorandum of the United States, Section E; Information, *united States of America v. Warner-Lambert Company LLC*, United States District Court, District of Massachusetts, May 13, 2004 (hereafter "Information") ¶¶ 8 - 10.

launch.[82] Warner-Lambert began seeking FDA approval for some indications, such as monotherapy for seizures, pediatric adjunctive treatment for seizures, and post-herpetic neuralgia. But FDA approval typically required expensive and time-consuming, randomized controlled double-blind clinical trials, which always carry the risk of demonstrating a negative (or inconclusive) effect. Despite conducting clinical trials in the United States and abroad, neither Warner-Lambert nor later Pfizer was ever to receive approval for Neurontin monotherapy indications.[83]

40. After evaluating the potential markets for other clinical uses, such as treatment of bipolar disorder, painful diabetic neuralgia, and chronic pain,[84] Warner-Lambert calculated that seeking FDA approval would not be worthwhile because of the expense of clinical trials, the short remaining patent life for Neurontin and the potential adverse impact on the sales of a new drug that Warner-Lambert was developing.[85] Warner-Lambert decided to promote off-label uses of Neurontin even though off-label promotion is expressly prohibited by the FDA.[86]

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[82] Information, ¶¶ 11-13; Sentencing Memorandum of the United States, pp. 13-17. See, e.g., Deposition of John M. Knoop, *United States v. Pfizer Inc., and Parke-Davis*, Case No. 96-11651-PBS, September 25, 2002 (Knoop Deposition), pp. 27-28 and 225-255; Memorandum from Mi Dong to Neurontin (Anticonvulsant) Development Team of 11/7/94, X029017-25; Memorandum from Mi Dong to Neurontin Development Team of 1/19/95, X028970-75 at pp. X028974-75; Memorandum from Mi Dong to Neurontin Development Team of 2/28/95, X028965-69 at X208969; Deposition of John Boris, *United States v. Pfizer Inc. and Parke-Davis*, Case No. 96-11651-PBS, September 16, 2002 (Boris Deposition), pp. 17-21; and Marketing Assessment: Neurontin in Psychiatric Disorders of 5/18/95, V090836-77.

[83] Marino deposition, pp. 69-70.

[84] Information ¶¶ 11-16. See also: *United States ex rel. Franklin v. Parke-Davis*, 147 F. Supp.2d 39 (D. Mass. 2001), Exhibit 27. [Parke-Davis memo from Francie Kivel to "Distribution," re: "Minutes from August 9, 1995 Neurontin Indications Decision Analysis Group Meeting"]; 29 August 1995: V049269-V049274 at 71. ("The indications to be investigated in the first phase of this analysis will be neuropathic pain, social phobia, panic, and bipolar disorders. ALS and spasticity will be examined subsequently.")

[85] The new drug was pregabalin. See, e.g., Memorandum from Mi Dong to Neurontin Anticonvulsant Development Team of 3/16/95, X028957-62 at p. X028961; Memorandum from J. Pieroni to Anton, Brandner, Cadre, Evans, Gemelli, Montgomery, and Summers of 3/22/95, V086787-92 at V086789; Interoffice Memorandum from Pande to Boris of 3/23/95, X029226; Cover letter from Brandicourt to Development Team of 7/31/95 with attached Marketing Assessment: Neurontin in Neuropathic Pain and Spasticity of 7/24/95, WL 07524-47 at WL 07524; Memorandum from Boris to Neurontin Pharmaceutical Sector Marketing Group of 7/31/96, V082736-61 at V082737; Marketing Assessment: Neurontin in Psychiatric Disorders of 5/18/95, V090836-77; and Memorandum from Francie Kivel to J. Boris, O. Brandicourt, E. Guerrero, J. Knoop, L. Magnus-Miller, and L. Perlow, October 26, 1995, V053848-77 at V053853.

[86] Information, ¶¶ 5, 19, 23-4, 27-8, and 34. See, e.g., Knoop Deposition, p. 35; and Deposition of James Parker, *United States v. Pfizer Inc., and Parke-Davis*, Case No. 96-11651-PBS, May 17, 2002 (Parker Deposition), pp. 136-37.

41. Warner-Lambert also encouraged the use of Neurontin at higher dosages than those approved by the FDA. Neurontin was approved for dosages from 900 to 1800 mg, but doctors were encouraged to use larger doses of up to 4800 mg, particularly for off-label uses, such as pain.[87] Although Warner-Lambert promoted the existence of a dose-response relationship for Neurontin,[88] the company had gathered substantial evidence that there was no clinical benefit to higher dosages.[89]

42. The strategy for the marketing and promotion of Neurontin for off-label uses was sophisticated, comprehensive and well coordinated.[90] Warner-Lambert employed a range of marketing and promotional techniques to promote off-label uses of Neurontin. Among them were the use of sale representatives,[91] medical liaisons,[92] consultants meetings and advisory boards,[93] and teleconferences.[94]

43. During sales calls to doctors, Warner-Lambert sales representatives encouraged doctors to prescribe Neurontin for a variety of off-label uses[95] even when there was no evidence to support claims of effectiveness or when studies had shown that the drug was not effective.[96] Free samples of Neurontin were given to doctors to encourage them to prescribe Neurontin for off-label treatments for new patients.[97]

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[87] See, e.g., AED Advisory Board Presentations of 11/8/95, 0008597-608 at 0008605; Memorandum from A. Spalding to J. Knoop and A. Crook of June 12, 1996, X005384-86 at p. X005384; Neurontin 1996 SE CBU Plan, W 003095-109 at p. W 003103.

[88] WLC_FRANKLIN_0000038501-02

[89] See, e.g., Letter from Department of Health & Human Services, Food and Drug Administration, to Parke-Davis of August 26, 1997; Memorandum form Mi Dong to Neurontin Development Team of November 30, 1995, X028920-24; Core Marketing Team Meeting 4/8-9/97 V047116-29 at V047121; and Parke-Davis Memorandum to distribution of October 2, 1997 with attached Minutes of Core Marketing Team Meeting V042352-63 at V042353.

[90] For comprehensive reviews, see, e.g., Sentencing Memorandum of the United States; Steinman et al., "The Promotion of Gabapentin: An Analysis of Internal Industry Documents," and Information.

[91] Information, ¶¶ 20-22.

[92] Information, ¶¶ 23-24.

[93] Information, ¶¶ 25-32.

[94] Information, ¶¶ 33-36.

[95] Information, ¶¶ 20-22.

[96] See, for example, Memorandum from J. Rizzo to J. Knoop/E. Guerrero, of October 20, 1995 V091388-9 at V091389.

[97] See, for example, 1998 Strategic Plan and A&P Allocation Grid V063424-27.

44. Using outside contractors as well as its own staff, Warner-Lambert organized meetings and events, including expensive dinners and conferences in luxury hotels, to promote off-label uses and higher dosages for Neurontin to doctors. At these events, both company representatives and paid consultants made false claims about Neurontin, concealed negative studies, and failed to present research findings in a balanced manner as required by regulations.[98]

B. Marketing Masquerading As Research: The Publications Strategy

45. Research and publications on Neurontin formed the basis of the marketing strategy for the drug.[99] In some cases, such as monotherapy for epilepsy, Warner-Lambert supported research into clinical uses for Neurontin to further company efforts to obtain FDA approval for new indications. In others, the company used "research" to promote unapproved uses for Neurontin, such as neuropathic pain and bipolar disorders, which Warner-Lambert had determined offered the greatest revenue potential.[100]

1. Sponsored Research, Grants and Studies and Medical Education and Communication Companies

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[98] See, e.g., Steinman et al., Emerging Applications in the Uses of AEDs, An Educational Proposal prepared for Parke-Davis by Professional Postgraduate Services, September 6, 1996, V057651-92.

[99] "Execute publication/educational plan and clinical trials program to support product expansion in emerging uses . . . Execute publication/educational promotional plan to expand earlier Neurontin use for epilepsy (i .e . monotherapy launch, QOL, data , STEPS, etc.)" *United States ex rel. Franklin v. Parke-Davis*, 147 F. Supp.2d 39 (D. Mass. 2001), Exhibit 40. Neurontin Northeast CBU [customer business unit] 1997: X001884-X001900 at 85 and 98. "Execute publication/educational promotional plan to expand earlier Neurontin use for epilepsy (i .e . montherapy launch, QOL data, STEPS, etc .)" *Ibid.*, at 90 and 98.

[100] "The advantages and disadvantages of various approaches to publication were discussed, ie, *[sic]* a single, well-controlled study vs. two well-controlled studies vs./in addition to Phase IV programs, etc.. *[sic]* It was also noted that we will publish negative study results, although it was noted that negative results would only impact the epilepsy market if a major safety concern was evidenced (unlikely, <5% chance). It was proposed that the options of the most interest in terms of this analysis would be investigating 1) the impact of a single, well-controlled study, and 2) the impact of two well-controlled studies." *United States ex rel. Franklin v. Parke-Davis*, 147 F. Supp.2d 39 (D. Mass. 2001), Exhibit 27. [Parke-Davis memo from Francie Kivel to "Distribution," re: "Minutes from August 9, 1995 Neurontin Indications Decision Analysis Group Meeting"]; 29 August 1995: V049269-V049274 at 70. "Bipolar disorders is the indication most favored for future study based on expected NPV and the general location of the NPV distribution . . . While the median NPV for neuropathic pain is approximately $34M less than for bipolar disorders ($76M vs $42M), the maximum potential NPV is approximately $16M higher for neuropathic pain ($93M vs $77M). Revisions to the forecast parameters resulted in a large shift in the NPV distribution for neuropathic pain. It may be valuable to consider these parameters further if clinical investigation of neuropathic pain is to entirely supplant the investigation of bipolar disorders." *United States ex rel. Franklin v. Parke-Davis*, 147 F. Supp.2d 39 (D. Mass. 2001), Exhibit 29. [Parke-Davis memo from Francie Kivel to "Distribution," re: "Neurontin Indications Publication Analysis Report"]; 26 October 1995: V053848-V053877 at 52.

46. Using outside medical education and communication companies, Warner-Lambert sponsored research,[101] prepared journal articles based on and paid researchers to put their names on those articles. These companies were hired to write the articles and find the authors.[102] Articles sponsored by a medical education company tended to report favorable conclusions about Neurontin, but the sponsorship was often not disclosed.[103]

C. Marketing Masquerading As Education: The Dissemination Strategy

47. "Medical education drives this market!!"[104] noted one Warner-Lambert business plan. Educational activities traditionally considered independent of marketing activities were used to promote Neurontin. Among them were teleconferences, accredited continuing medical education, sponsored educational meetings and conferences, advisory boards and consultants meetings, and medical liaisons.[105]

1. "Peer-to-Peer Selling"

48. Warner-Lambert recruited physicians who had the potential to influence Neurontin prescribing behavior among their colleagues to serve as speakers in

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[101] Steinman et al., pp. 288-290 (includes example of STEPS (Study of Neurontin: Titration to Effectiveness and Profiles of Safety) involving more than 700 physicians who enrolled an average of three patients each and received a $300 payment for each patient enrolled)

[102] "I am writing to provide you with both editorial status and billing status of the manuscripts we have been developing for the Northeast Customer Business Unit of Parke Davis for 1996 . . . these physicians are clinicians rather than academicians or Researchers . . . Enclosed please find a list of our work in process for you, along with a detailed status report on each." *United States ex rel. Franklin v. Parke Davis*, 147 F. Supp.2d 39 (D. Mass. 2001), Exhibit 64. [Letter from Jacki Gordon (AMM/Adelphi, Ltd) to Phil Magistro (Parke-Davis), re: development of manuscripts for Parke-Davis Northeast Customer Business Unit]; 8 November 1996:X005102-X005110 at 102. "We anticipate that by year's end, you will have several manuscripts submitted to journals as well as either a paper or poster accepted for the AAN." *Ibid.* at 105. Two marketing firms were offered $12,000 for each of 12 journal articles that they prepared. (Liz Kowalczyk, "Use of Drug Soars Despite Controversy," Boston Globe, November 25, 2002, A1, Pfizer_LKnapp_0091179-82 at 81; Melody Peterson, "Suit Says Company Promoted Drug in Exam Rooms," New York Times, May 15, 2002, C1. The company also apparently paid academic "authors" $1000 to sign them. (Melody Peterson, "Suit Says Company Promoted Drug in Exam Rooms," New York Times, May 15, 2002, C1.) See V06967326 at 74: "author interested; still playing phone tag. … [OUR COMPANY] HAS DRAFT COMPLETE, WE JUST NEED AN AUTHOR." (cited in Liz Kowalczyk, "Drug Company Pushed on Doctors Disclosed," Boston Globe, May 19, 2002, A1.) See also Steinman footnotes 92-98.

[103] Steinman et al., "Promotion of Gabapentin", page 289.

[104] Neurontin 1996 SE CBU [customer business unit] Plan: WLC_CBU_038946.

[105] See Information, ¶¶ 19-36

"peer-to-peer selling" programs.[106] These included local champions, who were seen as "one of the most effective ways to communicate our message,"[107] and "opinion" or "thought leaders," who were influential physicians affiliated with major medical centers.[108] Many of these leaders received substantial payments in honoraria, research grants, or educational grants.[109]

2. Continuing Medical Education, Sponsored Educational Meetings and Conferences

49. Warner-Lambert conducted teleconferences with paid physician monitors and small groups of physicians.[110] Although presented as educational events,[111] an internal company memo noted that "the key goal of the teleconferences was to increase Neurontin new prescriptions by convincing non-prescribers to begin prescribing and current prescribers to increase their new prescription behavior."[112]

50. Doctors were recruited and trained as Neurontin advocates at speaker bureaus and related physician-to-position programs.[113] To improve "public relations within the neurology community, etc., as well as [to impact] the volume of Neurontin new prescriptions," Warner-Lambert created a lecture series.[114]

51. In addition to directly sponsoring medical educational events, Warner-Lambert funded "unrestricted educational grants" to medical education and communications companies that create physician conferences on behalf of

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[106] See V058083-95, Northeast CBU 1997 Situation Analysis, 31 May 1996. See also Steinman footnote 19, "Business Strategies to Penetrate the Hospital Segment of the Northeast Consumer Business Unit"; "1998 Neurontin Tactics (Prepared by Cline, Davis & Mann) 30 July 1997" X005926-50; "Neurontin Northeast CBU 1997" X001884-900.

[107] See V058083-95 at 91, "Northeast CBU 1997 Situation Analysis", 31 May 1996.

[108] "in two documents Parke-Davis identified 40 potential follow leaders in the northeastern United States, including 26 current or future department chairs, vice chairs, and directors of academic clinical programs or divisions." (Steinman et al., page 285);

[109] Steinman et al., pp. 285 – 286 and and footnote 11. ("Of [40 potential thought leaders], 35 participated in at least one Parke-Davis-sponsored activity, including 14 who requested or were allocated $10 205 to $158 250 in honoraria, research grants, or educational grants between 1993 and 1997.")

[110] Steinman et al., page 286, Information, to pages 11-12. Warner-Lambert also set the agenda and surreptitiously monitored the teleconferences in some cases. (Steinman et al., based 286; Steinman footnotes 35, 36, 37,11,33)

[111] Steinman et al., footnote 33

[112] Steinman et al., footnote 34

[113] Steinman et al., page 286 (Steinman footnotes 19,25, 26, 28,38)

[114] Steinman et al., page 286, (Steinman footnotes 26, 28,38)

pharmaceutical companies and are often subsidiaries of marketing firms.[115] Because the grants were "unrestricted," Warner-Lambert officially relinquished control over the program, allowing speakers and participants to discuss unapproved uses of Neurontin and for participants to receive continuing medical education credit from the Accreditation Council of Continuing Medical Education (ACCME), which was not permitted for events directly sponsored by Warner-Lambert.[116] In practice, Warner-Lambert influenced the content as well as the selection of speakers and participants to promote off label uses of Neurontin at some of these events.[117] The company also tracked doctor's prescriptions to see if they prescribe Neurontin more after the meetings or after they were hired to speak about the drug.[118]

52. Unrestricted grants also paid for the costs of doctors to attend conferences and funding 75,000 copies of epilepsy handbook to high prescribers of anticonvulsant agents.[119]

3. Advisory Boards and Consultants Meetings

53. Warner-Lambert promoted off label uses of Neurontin through advisory boards and consultants meetings,[120] whose faculty may have been vetted by the company.[121] Warner-Lambert reserved the right "to probe the faculty further to definitively establish presentation contents and make the appropriate changes and/or recruited alternate speaker"[122] [Memo from Bina O'Brian, 24 June 1997 56]

54. Participants at one meeting were selected based on their high prescription rates[123] and "were delivered a hard-hitting message about Neurontin."[124] Company sales representatives tracked their prescribing behavior before and after the event.[125]

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[115] Steinman et al., page 287, (Steinman footnotes 41-44)

[116] Steinman et al., p. 287 (Steinman footnotes 45-48)

[117] Steinman et al., p. 287-288 (Steinman footnotes 32,49,51, 56-59, 61, 63)

[118] See, e.g., Steinman et al., p. 287-288.

[119] Steinman et al., p. 288.(Steinman footnotes 64, 65)

[120] Information, ¶¶ 25-32. Steinman et al., p. 288.

[121] Steinman et al., p. 284 (Steinman footnote 56)

[122] Steinman et al., p. 288 (Memo from Bina O'Brian, 24 June 1997 as cited in Steinman footnote 56)

[123] Steinman et al., p. 288 (Steinman footnote 17)

[124] Steinman et al., p. 288 (Steinman footnote 71)

[125] Steinman et al., p. 288 (Steinman footnote 70)

55. Participants received honoraria and paid travel, lodging, and amenities at the resorts of luxury hotels where the events were occurred.[126] Some faculty participants also received honoraria and grants for participating[127] and may have been vetted in advanced by Warner-Lambert for favorable views of Neurontin.[128]

56. Company reserves the right "to probe the faculty further to definitively establish presentation contents and make the appropriate changes and/or recruited alternate speaker."[129]

4. Medical Liaisons

57. Medical liaisons are meant to be neutral, scientific experts on a drug company's products.[130] Although sales force representatives are not permitted to promote off-label uses of the drugs they sell, the FDA does allow drug company medical liaisons to provide balanced, truthful information regarding off-label usage in response to an unsolicited, specific request from a doctor. Warner-Lambert used medical liaisons to promote Neurontin for unapproved uses.[131]

5. Targeting Residents

58. In an effort "to influence physicians from the bottom up" and "to solidify Parke-Davis' role in residents' mind as he/she evolves into a practicing physician,"[132] the Warner-Lambert targeted residents with, among other things,

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[126] Steinman et al., p. 288, Steinman footnotes 51 (Letter from Timothy Lynch, 20 August 1996), 52 ("Neurology Update: Anticonvulsants-Original Consultants Meeting, Boston"), 71-76(Jupiter Beach, Atlanta and other meetings)

[127] Steinman et al., p. 288 (Steinman footnotes 11, 52, 71, 73)

[128] Steinman et al., p. 288, Steinman footnote 56 ("it is [our] policy to complete a literature search to determine who will author is favorable articles on the topics outlined" [Memo from Bina O'Brian, 24 June 1997); Company reserves the right "to probe the faculty further to definitively establish presentation contents and make the appropriate changes and/or recruited alternate speaker" [Memo from Bina O'Brian, 24 June 1997]

[129] Memo from Bina O'Brian, 24 June 1997

[130] Sentencing Memorandum of the United States, Page 11.

[131] Information, ¶ ¶ 23-24. One Warner-Lambert Medical Director put it this way:

> What we'd like you do is, anytime you're called out just make sure that your main focus out of what you're doing is on Neurontin … When we get out there, we want to kick some ass, we want to sell the Neurontin on pain. All right? And monotherapy and everything that we can talk about, that's what we want do.

Information, ¶ 24.

[132] Business Strategies to Penetrate the Hospital Segment of the Northeast Consumer Business Unit from Steinman footnote 24

"resident programs," a video case series and a "CNS [central nervous system] residence course."[133]

VII. Marketing Neurontin in the Pfizer Era (2000 – 2004)

After acquiring Warner-Lambert in June 2000, Pfizer appears to have continued the publication strategy and off-label promotion initiated by Warner-Lambert's Parke-Davis subsidiary. Pfizer's marketing and promotional efforts, like those of Warner-Lambert before it, were significant contributing factors to the off-label sales of Neurontin.

A. Pfizer Continued the Off-Label Promotion of Neurontin

59. Like Warner-Lambert, Pfizer had strong economic incentives to continue promoting off-label uses of Neurontin. Pfizer company documents, business plans and marketing plans reveal that sales for epilepsy were declining and constituted only about 10 percent of all Neurontin sales,[134] that the majority of Neurontin sales were for unapproved uses, and that unapproved uses for Neurontin presented the largest and most attractive markets.[135] Even though approved uses of Neurontin comprised less than 15 percent of its total sales, Pfizer set and met ambitious goals for Neurontin sales growth that could not reasonably be met by growth in approved uses alone.[136]

60. An analysis of Pfizer's marketing budgets for Neurontin confirms the importance of its off-label sales. Pharmaceutical companies typically spend most of their marketing budgets on sending the sales representatives to visit doctors. Pfizer apparently spent the largest share of its Neurontin marketing budget on medical education.[137] This is consistent with Pfizer's alleged strategy of promoting off-label uses for Neurontin. Although drug company sales representatives are prohibited from discussing unapproved drug uses in sales calls, off-label uses can be discussed at independent medical education events.

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[133] Strategic Plan and A&P Allocation Grid, 27 August 1997 from Steinman footnote 13

[134] Sales of Neurontin for adjunctive epilepsy therapy were its only approved use until its approval for postherpetic neuralgia in 2002.

[135] In an internal Pfizer slide presentation, the question was asked, "Knowing what we know now, and if we could start all over in the US, how might the US develop Neurontin?", and the presentation's answer is that the only indication for Neurontin Pfizer would "[p]robably not" pursue is epilepsy. Pfizer_LTive_0006484-97, at Pfizer_LTive_0006490.

[136] Marino Deposition, pp. 382-88, 529-31.

[137] Compare Neurontin 2001 U.S. Operating Plan, Pfizer_RGlanzman_0000669 (Medical Education $38.0 million for 2001 LE and $28.3 million for 2001 BUD) with Neurontin 2001 Operating Plan, Pfizer_LTive_0008259 (Field Force $16 million for 2001 LE).

61. Evidence shows that to meet these goals, Pfizer continued the publication strategy, continued to suppress and delay publication of clinical studies and data regarding Neurontin's lack of efficacy, and continued to promote articles advocating Neurontin for unapproved uses without disclosing that Neurontin was not effective for those uses. The Neurontin 2001 U.S. Operating Plan, for example, identified a key issues as the "Unsatisfied Market in Emerging Uses" – that is, unapproved, off-label uses[138] – and proposed to "Meet Demand for Medical Education from Medical Community" as a strategic response.[139]

62. One example of the suppression and delay in publication of a negative clinical study concerns a failed diabetic peripheral neuropathy trial (study 945-224) conducted by Dr. Reckless in the United Kingdom.[140] Concerns that these results would damage Neurontin sales both for diabetic peripheral neuropathy and neuropathic pain generally apparently led Pfizer to suppress the Reckless study by delaying its publication[141], to preclude Dr. Reckless from writing the article himself, to hire an outside consulting firm to cast his study in a more favorable light[142], and, in the end, to withdraw support for the article.

63. To produce and manage publication of journal articles about Neurontin and its off-label uses, Pfizer engaged Medical Action Communications, Inc. (MAC). One goal was to increase the number of off-label publications, according to company documents. Of 12 manuscripts published in 2001, MAC reported that 5 pertained to epilepsy, 4 to neuropathic pain and one to substance abuse, the last two being unapproved uses for Neurontin.[143] For 2002, Pfizer planned to

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[138] Emerging uses means unapproved or off-label uses. Marino deposition, pp. 119 – 120, 194.

[139] Neurontin 2001 U.S. Operating Plan, Pfizer_RGlanzman_00000677.

[140] Another example of a negative study that was delayed by Pfizer is the POPP study. See Pfizer_JMarino_0000703-4, Pfizer_JMarino_0000809, and Pfizer_RGlanzman_0134501-3.

[141] From E-mail of John Marino, Pfizer Neurontin World Wide Team Leader: "We must delay the publication of -224, as its result were not positive (*sic*)." Pfizer_LCastro_0002678-82, at Pfizer_LCastro_0002680. See also, Pfizer_JMarino_0000809, Pfizer_LeslieTive_0020985-6 and Pfizer_LeslieTive_0080783-4.

[142] "I think that we can limit the potential downsides of the 224 study [Reckless Study] by delaying the publication for as long as possible and also from where it is published. More importantly it will be more important to how WE write up the study. We are using a medical agency to put the paper together which we will show to Dr Reckless. We are not allowing him to write it up himself." (Emphasis in original.) Pfizer_LeslieTive_0020985-6.

[143] Neurontin Publication Subcommittee Current Status and 2002 Plans 09-January 02, Pfizer_SDoft_0026365.

increase the number of manuscripts published, submitted or planned for submission to 17, of which 4 related to epilepsy, 7 to neuropathic pain, 3 to movement disorders, and one each to migraine and hot flashes.[144]

64. Pfizer's marketing plans set out goals for the dissemination of sponsored articles and research to doctors at scientific meetings, conferences, and continuing medical educational events.[145] To achieve its goals, Pfizer continued to engage outside medical education communications companies to identify and promote "key messages"[146] in articles and presentations about Neurontin to target audiences.[147] As John Marino, Pfizer's Worldwide Team Leader for Neurontin, admitted, "[i]t's tough to distinguish" marketing tactics from medical education programs.[148]

65. Pfizer apparently continued to suppress clinical information and data regarding Neurontin's lack of efficacy. From the clinical trials conducted by Dr. Reckless[149] and Dr. Gorson[150], Pfizer was aware that Neurontin was ineffective for neuropathic pain. Pfizer was also aware that Neurontin was ineffective for neuropathic pain from internal consultant meetings.[151] Yet, rather than listening to the consultant physicians' feedback, the Neurontin team rewrote the minutes of the meetings[152] to "support [their] case"[153] for pursuing the use of Neurontin for neuropathic pain. Pfizer was aware that Neurontin was ineffective for nociceptive pain.[154]

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[144] Neurontin Publication Planning 2003: Introduction by Alison Fannon, Pfizer_AFannon_0002934.

[145] See, e.g., Neurontin Publication Planning 2003: Introduction by Alison Fannon, Pfizer_AFannon_0002912-67.

[146] See, e.g., Neurontin Publication Subcommittee Current Status and 2002 Plans 09-January 02, Pfizer_SDoft_0026347-49; Pfizer_LTive_0009300-27.

[147] "The Challenge … Ensure consistent implementation of key medical and marketing messages in support of Neurontin for each target indication with the various target audiences." Neurontin Publication Subcommittee Current Status and 2002 Plans 09-January 02, Pfizer_SDoft_0026340. See also Neurontin Publication Subcommittee Current Status and 2002 Plans 09-January 02, Pfizer_SDoft_0026346.

[148] Marino deposition, p. 186.

[149] Pfizer_LCastro_0002678-82, Pfizer_JMarino_0000809 and Pfizer_LeslieTive_0020985-6.

[150] Marino deposition, pp. 243-246.

[151] Pfizer_LKnapp_0009569-73, Pfizer_JMarino_0000363-7, and Pfizer_JMarino_0000153-7.

[152] Pfizer_JMarino_0000153-7 and Pfizer_LKnapp_0070556-8.

[153] John Marino wrote to Steve Piron in an E-mail after a Pfizer Global Development Review Committee meeting about Neurontin: "Now it looks like we have to rewrite the minutes to support our case. Want to take a shot at it?" Pfizer_JMarino_0000153-7, at Pfizer_JMarino_0000153.

[154] Marino deposition, pp. 246-247.

B. Health & Human Services Determinations that Pfizer's Representations About Neurontin Are False And Misleading

66. An example of Pfizer's inappropriate, off-label promotion of Neurontin was identified by the FDA's Division of Drug Marketing, Advertising and Communications (DDMAC).[155] On July 1, 2002, Dr. Lisa L. Stockbridge, PhD., a Regulatory Reviewer at DDMAC, notified Pfizer that certain Neurontin marketing material was "in violation of the Federal Food, Drug and Cosmetic Act . . . because [Pfizer] makes representations about Neurontin that are false and misleading."[156] Specifically, DDMAC objected to Pfizer marketing material suggesting 1) that the mechanism of action of Neurontin in the human brain had been established when this was false, as the mechanism by which Neurontin worked was unknown; 2) that "Neurontin is useful for a broader range of CNS [central nervous system] conditions that has been demonstrated by substantial evidence"; and 3) that "Neurontin can be used as monotherapy for various CNS disorders" when Neurontin was only approved as adjunctive therapy in the treatment of partial seizures and adult and pediatric patients.[157] Because these representations about Neurontin were false or misleading, DDMAC requested that Pfizer "[i]mmediately discontinue the use of [these] and any other promotional material with the same or similar issues."[158]

VIII. Effects of Neurontin Off-Label Marketing Strategy

67. Even if Pfizer had done nothing to promote unapproved uses of Neurontin after it acquired Warner-Lambert, sales of Neurontin for unapproved uses would have continued. Successful marketing, in general, and pharmaceutical marketing, in particular, has long term effects. The creation of a successful brand image leads to sales even after promotion stops.

A. Marketing Effects Are Long-Lived

1. Evidence from Academic Studies

68. The effect of marketing on drug sales has been widely studied over the years. Empirical studies have investigated the responsiveness of drug sales to

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[155] Lisa Stockbridge Letter, dated July 1, 2002, Pfizer_LCastro_0074739-40. For another example, see Lisa Stockbridge Letter, dated June 29, 2001, Marino Exhibit 45, Pfizer_RGlanzman_0054596-609.

[156] Lisa Stockbridge Letter, dated July 1, 2002, Pfizer_LCastro_0074739-40.

[157] Ibid.

[158] Ibid. at Pfizer_LCastro_0074740.

both the drug company and its competitors marketing expenditures. Examples of recent research include work by Berndt *et al*. (1995), Gonul (2001), King (1997), Manchanda et al. (2000), and Rizzo (1999).[159] Some of these studies use aggregate data while others rely on physician-specific data. The results of this research show that sales calls and free samples have significant positive effects on the number of prescriptions for a drug.

69. Although specific results vary across drugs and studies, the response of drug sales to promotional activities is well established. Multiple academic studies also show that the effects of marketing and promotional are long-lived, with estimated depreciation rates for marketing and promotional stocks near zero.[160] Once doctors learn about a drug and are motivated to try it, they tend to remember and stay with the drug.

2. Evidence from Sales Calls

70. An analysis of company sales call data reveals the effect these calls had in promoting off-label uses of Neurontin. I understand that psychiatrists have little reason to prescribe Neurontin to their patients for its approved uses and that nearly all prescriptions written by psychiatrists for Neurontin will therefore be for off-label uses.

71. For sample of 832 psychiatrists, company sales call records were matched with their history of Neurontin prescriptions.[161] Figure 9 shows that both new

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[159] See, e.g., E.R. Berndt, L. Bui, D. Reiley and G. Urban, "Information, Marketing and Pricing in the U.S. Anti-Ulcer Drug Market," American Economic Review, Vol. 85, No. 2, pp. 100-105, May 1995 (cumulative spending on both medical journal and physician detailing increases drug sales and market-expanding promotion (e.g., marketing that increases awareness of the existence of a new use for a drug) depreciates slowly); F. Gonul, F. Carter, E. Petrova and K. Srinivasan, "Promotion of Prescription Drugs and Its Impact on Physician Choice Behavior," Journal of Marketing, 65:3, pp. 79-90, 2001; C. King, III, "Marketing, Product Differentiation and Competition in the Market for Antiulcer Drugs," Boston MA: Harvard Business School Working Paper No. 01-014, 2000 (http://papers.ssrn.com/sol3/papers.cfm?abstract_id=891128); P. Manchanda, and P. Chintagunta, "Responsiveness of Physician Prescription Behavior to Salesforce Effort: An Individual Level Analysis", *Marketing Letters*, Vol. 15, July 2004, pp. 129-45; J. Rizzo, "Advertising and Competition in the Ethical Pharmaceutical Industry: The Case of Antihypertensive Drugs," Journal of Law and Economics, 42:1, pp. 89-116, 1999 (both stocks and flows of sales force expenditures reduced price sensitivity over time because promotional expenditures create greater brand loyalty).

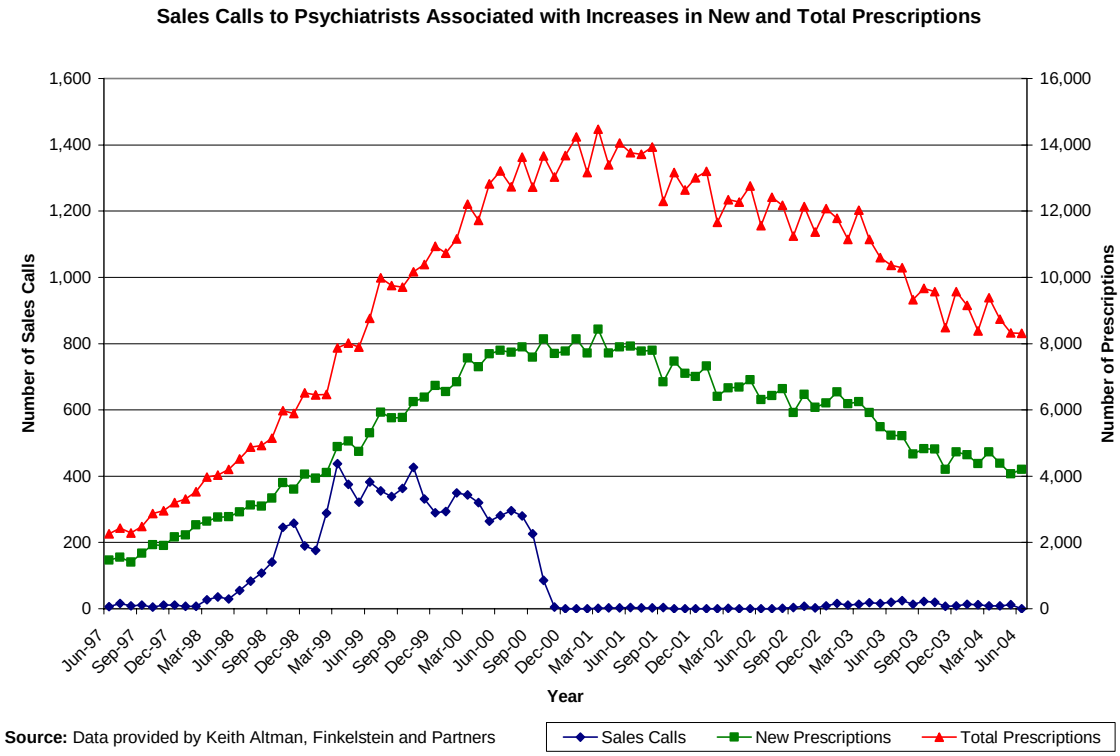
[160] See footnote 158.

[161] For 832 psychiatrists in the available data, it was possible to find an exact match between the company sales call record for the psychiatrist and the prescription record for that psychiatrist based on first name, last name, street address, and ZIP code for the entire period for which complete data were available, June 1997 through June 2004, when generic competition entered the market for Neurontin. These 832 psychiatrists represent 3.5% percent of the 23,917 psychiatrists in the sales call data. It is not possible, to determine the proportion these prescriptions represent relative to all prescriptions written by all psychiatrists given the available data.

and total Neurontin prescriptions for these doctors increased after they received sales calls. The figure also shows that these doctors continued to prescribe Neurontin years after receiving their last sales call, revealing the long-term effects of pharmaceutical marketing.

72. Figure 9 shows that psychiatrists continued to write prescriptions for Neurontin even after Pfizer initially stopped sales calls to psychiatrists in 2001. Pfizer resumed sales calls to psychiatrists, although at a lower rate, in 2002, after Pfizer received approval for the postherpetic neuralgia indication for Neurontin. I understand that this is also not a condition likely to be treated by psychiatrists and that their prescriptions were likely to be off-label prescriptions, as were the bulk of Neurontin sales.

Figure 9: Sales Calls to Psychiatrists are Correlated with Increases in New and Total Prescriptions



Source: Data provided by Keith Altman, Finkelstein and Partners

B. Pervasive Influence of Neurontin Marketing

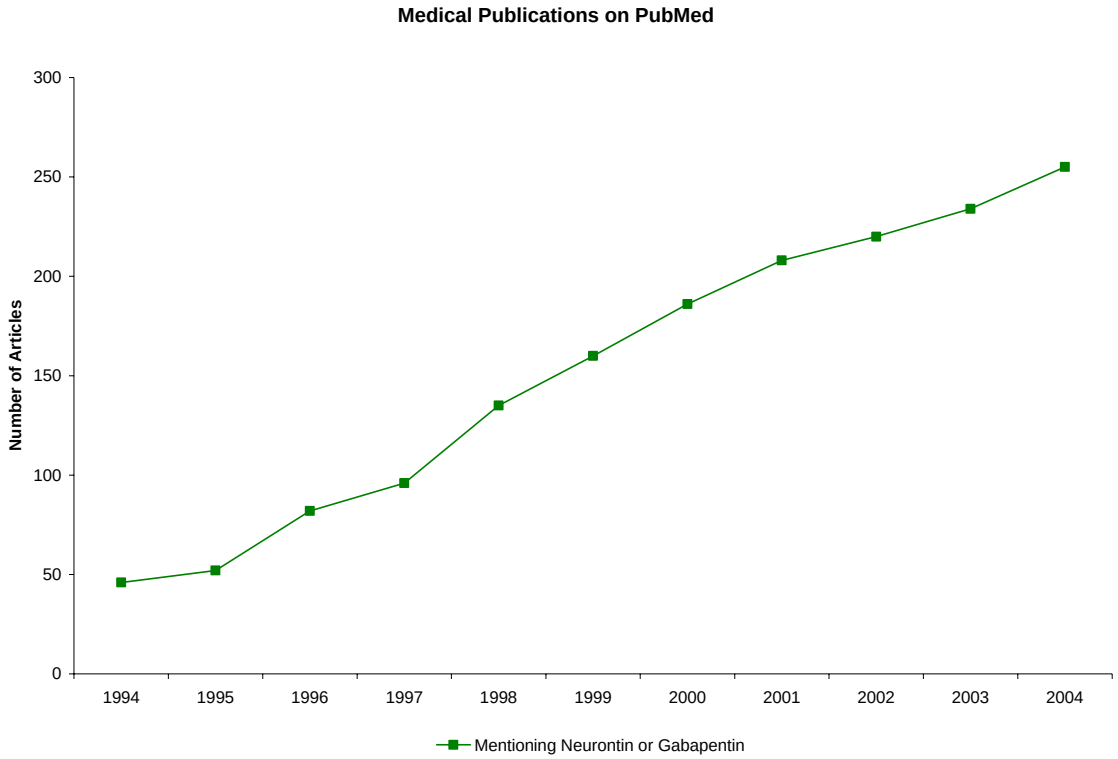
73. As demonstrated by the numbers of articles published about Neurontin, the sales calls, and the medical education events sponsored by Pfizer, Neurontin was a well-known and well-promoted drug.

1. Neurontin Publications

74. A simple count of the number of articles in the medical literature that mention either Neurontin or gabapentin reveals the growth and prevalence of Neurontin publications in the medical literature. Figure 10 presents the number of articles that contain the words Neurontin or gabapentin, or both, for each year from 1994, when Neurontin was first sold, to 2004, when generic versions of Neurontin entered the market, in the PubMed database, a standard reference.

75. From 1994 to 2000, the number of articles mentioning either Neurontin or gabapentin increases from under 50 per year to nearly 190 per year. After Pfizer takes over, the rate grows from 186 to 255 per year. Of the 1,674 articles from this period, the majority are published during the Pfizer era.

Figure 10: Large Increases in Medical Literature Mentioning Neurontin or Gapapentin



76. But many more were published worldwide. According to John Marino, Pfizer's Worldwide Team Leader for Neurontin, there were "8,000 publications done on [Neurontin] in the past decade … a substantial number."[162] Publications were one of "a variety of mechanisms [through which] word about unapproved indications was circulated," he said.[163]

2. Sales Calls

77. Given the number of sales calls that Pfizer proposed in its 2002 business plan, Pfizer would have reached large numbers of doctors. The business plan projects that Pfizer sales representatives would reach the majority of primary care physicians, neurologists, rheumatologists, and orthopedists, in addition to considerable percentages of other physician specialties.[164] The total sales call effort was estimated to reach 31% of all doctors. [165]

78. Figure 10 presents the total number of Neurontin sales calls made each month from January 1999 through May 2004. As the graph shows, the number of Pfizer sales calls beginning at the end of 2002 greatly exceeds those made by Warner-Lambert from 1999 to 2000.

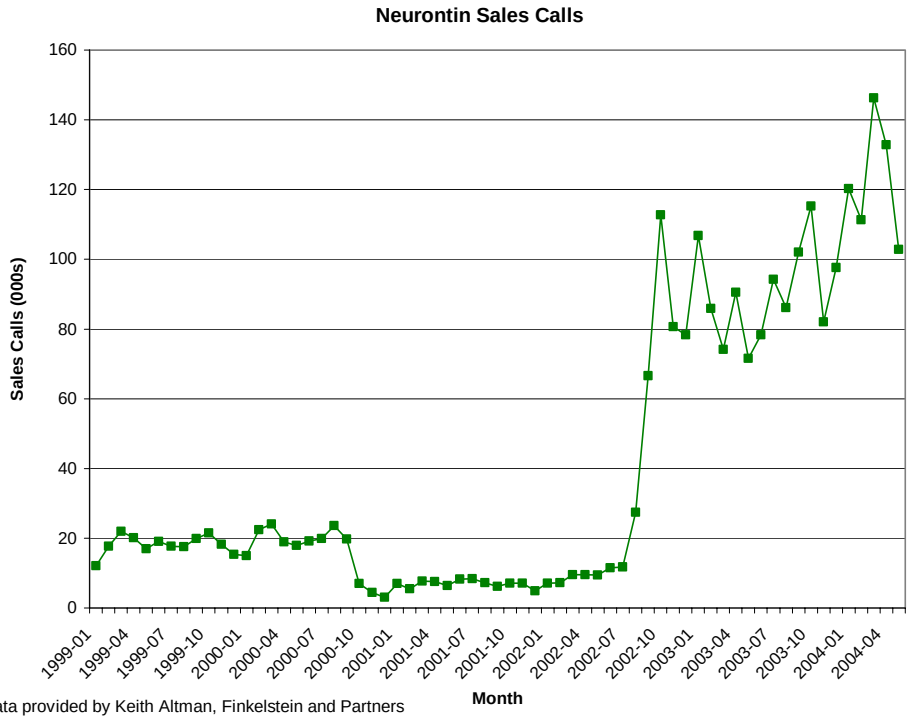
[162] Marino deposition, p. 251.

[163] Marino deposition, p. 251.

[164] Chart shows 2002 proposed detailing levels to cover 57% of the primary care physician universe, 64% of neurologists, and 69% of rheumotologists/orthopterists. Pfizer_LTive_0008275-92, at Pfizer_LTive_0008284.

[165] Pfizer_LTive_0008284

Figure 10: Number of Neurontin Sales Calls in 2003 Exceeds Number of Calls Between 1999 and 2000



Source: Data provided by Keith Altman, Finkelstein and Partners

3. Medical Education Programs and Conferences

79. Pfizer intended to reach and educate large numbers of doctors about emerging, or off-label, use of Neurontin through its medical education programs, as shown in Attachment C,

C. Indirect Influences

80. Most doctors likely would never have heard of Neurontin but for the off-labeling marketing efforts of Warner-Lambert and allegedly Pfizer. The inability to prove that Warner-Lambert or Pfizer contacted a doctor directly does not mean that that doctor was not influenced by Warner-Lambert and Pfizer marketing efforts. Pfizer's off-label marketing of Neurontin indirectly influenced all, or substantially all, doctors prescribing Neurontin in one of two ways. First, a doctor who did not have direct contact with Pfizer most likely was influenced in his prescribing habits by one who did. Second, all, or substantially all, doctors were indirectly affected by Pfizer's suppression of negative or adverse information about Neurontin that would have affected their prescribing habits.

81. It seems unlikely that a responsible doctor who was never heard of Neurontin would prescribe Neurontin for an off-label use without first consulting the medical and scientific literature, a colleague, or a medical reference work. I understand that to do so would be part of the doctor's professional and ethical responsibility.

82. Doctors work in an environment where informal communications among fellow doctors, or "word-of-mouth," play an important role in the dissemination of information about drugs and treatments. Colleagues are generally perceived as credible, independent, and reliable sources of information. Studies have shown that doctors learn extensively from and draw upon their colleagues' clinical experiences.[166] Indeed, academic research has found that "the source most influential and encouraging first prescribing [a] new drug … [is] colleagues."[167]

83. The academic literature has shown that social interactions among doctors can influence their prescribing behavior. Berndt et al., for example, find that brand-level network effects affect the rate at which a drug diffuses into the market. Widespread use of a drug implicitly conveys important information about its safety and efficacy, which increases word-of-mouth communications and accelerates the rate at which others become aware of and adopt the drug.[168]

84. Even doctors who did not receive visits from Neurontin sales representatives were more likely to prescribe Neurontin off-label because of indirect influences of Neurontin's extensive promotional efforts. The reason is that Neurontin promotional plans targeted the two areas physicians rely on most heavily for their information: publications and colleagues.[169] Thousands of papers were published about Neurontin (gabapentin),[170] which would have made it hard

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[166] Dale D. Christiansen and Albert J. Wertheimer (1979), "Sources of Information and Influence upon New Drug Prescribing among Physicians in an HMO," Soc. Sci. & Med., pages 313-322; Harikresh Nair, Puneet Manchanda, Tulidaa Bhatia, "Asymmetric Peer Effects in Physician Prescription Behavior: The Role of Opinion Leaders," Stanford Working Paper.

[167] Dale D. Christiansen and Albert J. Wertheimer (1979), "Sources of Information and Influence upon New Drug Prescribing among Physicians in an HMO," Soc. Sci. & Med., pages 313-322.

[168] Berndt, Pindyck and Azoulay, "Consumption Externalities and Effusion in Pharmaceutical Markets: Antiulcer Drugs," The Journal of Industrial Economics, June 2003, 243-270.

[169] A meta-analysis of twelve papers looking at physician preferences for information sources found that "physicians prefer to obtain information from journals and books, but also that they often consult colleagues to get answers to clinical and research questions." James Haug, "Physicians' preferences for information sources: a meta-analytic study", *Bull Medical Library Association*, Vol.85, July 1997.

[170] "As I mentioned, there were thousands and thousands, I think it was 8,000 to be exact, publications done on gabapentin in the past decade. It was a substantial number of publications that were created for

for a physician to not have heard about the product. The makers of Neurontin were well aware of these social networks[171] and hoped to exploit them through their marketing efforts.[172]

85. The widespread use of Neurontin[173] would further encourage doctors who may not have had direct contact with the drug company to prescribe the drug, because "widespread use of a drug may convey information about its safety and efficacy, and, for physicians, may imply 'accepted practice' and hence greater immunity to malpractice lawsuits. … [This] could lead to the dominance of one drug - not necessarily the most efficacious or safest - despite the availability of close substitutes."[174] This idea of high prescription volume signaling safety may have been especially relevant for Neurontin.[175] More important, as Neurontin sales increased year-over-year (See Figure 7), the indirect influences would have become stronger,[176] encouraging physicians to prescribe Neurontin, regardless of

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gabapentin, both independently, as well as within Pfizer, as well as Parke Davis." Deposition of John Marino (Marino Deposition), p. 251.

[171] Q. As a Worldwide Team Leader for Neurontin and marketing of Neurontin, is it your expectation that physicians talk to one another regarding their prescribing practices?

A. It's a natural medical practice for physicians to speak to each other about their prescribing habits and recommendations and decisions.

Marino Deposition, p.525.

[172] "Q. Is it your desired outcome as the Marketing Director, Worldwide Team Leader for Neurontin that when you distribute a marketing piece to a physician, that that physician shares that with a fellow physician in their practice?

A. In terms of promotional messages that are delivered by sales reps, yes, that would be the case." Marino Deposition, p.526.

[173] In 2000, Neurontin passed $1 billion in annual sales becoming an official block-buster drug (See Figure 7), and in 2003, Neurontin ranked 10th in U.S. sales (Drugs.com, http://www.drugs.com/top200_2003.html).

[174] Berndt, Pindyck, and Azoulay, "Consumption Externalities and Diffusion in Pharmaceutical Markets: Antiulcer Drugs", *The Journal of Industrial Economics*, June 2003, 243-270.

[175] At the 2002 Pfizer Expert Meeting, the panel concluded, "The success of gabapentin is not due to its efficacy, it is less efficacious than Tricyclic antidepressants (TCA), but is due to a more acceptable side effect profile." Pfizer_LKnapp_0070537-44, at Pfizer_LKnapp_0070539.

[176] "As more people use the product, word-of-mouth communication increases, accelerating the rate at which others become aware of it." Berndt et al. (2003), *Op. cite*., p.244.

whether or not they had direct contact with the company or received sales calls from Neurontin sales representatives.

86. Given the high levels of detailing proposed by Pfizer in 2002,[177] it is unlikely that a doctor would be completely unaware of Neurontin, especially in the specialties where Pfizer most heavily promoted Neurontin. Pfizer's Neurontin sales representatives visited the majority of primary care physicians, neurologists, rheumatologists, and orthopedists.[178] Since doctors share information[179] and rely on each other for new information, [180] any doctor who did not receive a personal visit would likely learn about Neurontin through a colleague who was visited.

87. Because it was perceived as "safe and efficacious", Neurontin was listed on nearly all formularies.[181] Neurontin's formulary status would have also created indirect influences encouraging prescriptions. If a doctor had a patient in need of treatment for one of the numerous off-label conditions for which Warner-Lambert and Pfizer promoted Neurontin, the physician may have prescribed Neurontin simply because it was on formulary, without ever having been personally contacted by the company or its sales representatives promoting Neurontin.

D. Failure to Disclose Negative Information About Neurontin

88. John Marino, Pfizer's Worldwide Team Leader for Neurontin, testified that Pfizer has an obligation to share negative results of its exploratory studies with the medical community[182] and that this was the practice at both Warner-

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[177] See Pfizer_LTive_0008275-92.

[178] Pfizer_LTive_0008284.

[179] Marino acknowledges that physicians discuss their prescribing with one another.

> Q. As a Worldwide Team Leader for Neurontin and marketing of Neurontin, is it your expectation that physicians talk to one another regarding their prescribing practices?
>
> A. It's a natural medical practice for physicians to speak to each other about their prescribing habits and recommendations and decisions."
>
> Marino deposition, p. 525.

[180] Haug, James, "Physicians' preferences for information sources: a meta-analytic study", *Bull Medical Library Association*, Vol.85, July 1997.

[181] "Neurontin is already on almost all formularies. Neurontin is perceived as safe and efficacious." Pfizer Neuropathic Pain PBM Advisory Board Executive Summary March 2002 (Pfizer_CGrogan_0005992-6002 at 005995)

[182] Marino deposition, p. 239.

Lambert and Pfizer.[183] To suppress or delay a negative study would be misleading and would not present a fair and balanced view, according to Mr. Marino.[184] "The pharmaceutical company's responsibility is to help teach physicians about the risk/benefit profile of appropriate therapies for treatment," including a full explanation of what the risks are, Mr. Marino further testified.[185]

89. Yet Pfizer allegedly took no affirmative action to disclose what it knew about problems with Neurontin. Pfizer never sent out "Dear Doctor" letters[186] informing doctors about the negative side-effects of Neurontin.[187]

90. Having spent considerable time and money communicating positive messages about Neurontin to doctors, Pfizer appears to have devoted fewer resources to re-educating doctors when the news about Neurontin was negative. In 2000, Pfizer scientists publish results of a negative study showing that Neurontin is not as effective as a placebo in treating bipolar disorder.[188] But by 2003, the new message about Neurontin's lack of efficacy for treating bipolar patients did not to appear to have taken hold among doctors, according to Dr. Gary Sachs, Director of the Harvard Bipolar Research Program at the Massachusetts General Hospital.[189] Pfizer's Worldwide Team Leader for Neurontin, John Marino, admitted that, as far as he was aware of, Pfizer has never sent out a "Dear Doctor" letter to physicians about Neurontin for the treatment of bipolar disorder or any other use.[190]

91. Leaving aside the question of whether Pfizer had an affirmative to duty to disclose negative information about Neurontin and to disseminate it among doctors, it is clear that withholding or delaying such negative information would

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[183] Marino deposition, p. 318.

[184] Marino deposition, pp. 318-319.

[185] Marino deposition, pp. 423-424.

[186] "Dear Doctor" letters are used by pharmaceutical companies and the FDA to alert physicians about drug safety.

[187] "Q. Have you ever initiated the sending of a "Dear Doctor" letter related to Neurontin?

A. No, I don't recall that -- that Neurontin has ever -- at least I have not personally been involved in sending out a "Dear Doctor" letter to physicians about Neurontin." Marino deposition, p. 475-476.

[188] Pande AC, Crockatt JG, Janney CA, Werth JL, Tsaroucha G. Gabapentin in bipolar disorder: a placebo-controlled trial of adjunctive therapy. Gabapentin Bipolar Disorder Study Group. Bipolar Disord. 2000;2:249-55. [PMID:11249802].

[189] NPR, The Selling of Neurontin by Snigdha Prakash, January 16, 2003

http://www.npr.org/templates/story/story.php?storyId=920362.

[190] Marino deposition pp. 475-76.

cause Neurontin sales for off-label uses to be greater than they would have been if the negative information had been disclosed where the negative information pertains to Neurontin's lack of efficacy for a particular use. Disclosure of negative information may also cause doctors to modify their behavior in other ways, such as more closely monitoring their patients, that would lead to better health outcomes.

E. Failure to Disclose Known Risks of Neurontin for Depressed and Bipolar Patients

92. Warner-Lambert and subsequently Pfizer were aware from the outset that Neurontin might be inappropriate for larger populations and posed serious potential risks for depressed and bipolar patients. According to the original clinical review of Neurontin by Cynthia G. McCormick, M.D.:

> Less common but more serious events may limit the drug's widespread usefulness. … depression, while it may be not an infrequent occurrence in the epileptic population, may become worse and require intervention or lead to suicide, as it has resulted in some suicidal attempts.
>
> In its critical database of 2048 patients, [Neurontin] has a risk profile that is uncertain, with five groups of important adverse events that have not been fully characterized, specifically, seizure exacerbation, carcinogenicity, clinically important depression, renal failure and teratogenicity. Accumulated long-range safety data are limited by the excess of attrition due to apparent lack of sustained efficacy.[191]

93. These concerns appear to have been the reasons that then Warner-Lambert researcher Dr. Atul Pande specifically excluded depressed patients from his study population in a trial of the use of Neurontin for bipolar disorder, a study that produced negative results: "So who were these people – the population for this study consisted of bipolar 1 patients and the only subset of the bipolar 1 patients that we excluded were people that were purely depressed. So their current state were either manic or hyper manic or mixed, but when we began this study, we had absolutely no evidence that [Neurontin] was likely to be antidepressant and therefore, we felt it *ethically unjustified* to include depressed patients. (emphasis added)"[192]

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[191] Pfizer_LAlphs_0084359-479 at 477.

[192] Statement of Atul Pande, M.D., F.R.C.P.C., "Combination Treatment in Bipolar Disorder, "Third International Conference On Bipolar Disorder, June 18, 1999.

94. I understand that doctors would consider this information material to their decisions to prescribe Neurontin and that it would have affected their behavior. I further understand that although the mode of action of Neurontin was unknown when the drug was originally approved, it is now known that Neurontin depletes serotonin and neuropinephrine and that low levels of these neurotransmitters are an established risk factor for depression and suicide.

F. Drug Risks Decrease Drug Sales

95. Known risks and side effects play an important role in the prescription of drugs. The FDA requires that most risks for drugs be listed on the drug's label or package insert. Doctors take them into consideration when choosing which drug to prescribe for a patient. Drug risks, side effects and adverse reactions with other drugs affect drug sales. Academic studies have shown that an increase in the number of adverse side effects listed reduces the drug's sales or market share, or both.[193] When bad news about drug side effects or interactions hits the market, sales for that drug typically fall.

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[193] *See, e.g.*, Ernst R. Berndt, Linda Bui, David R. Reiley and Glen Urban, "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," *American Economic Review* (1995), 85, 2, 100-105; E.R. Berndt, A. Bhattacharja, D.N. Mishol, A. Arcelus and T. Lasky, "An Analysis of the Diffusion of New Antidepressants: Variety, Quality, and Marketing Efforts," *Journal of Mental Health Policy and Economics* (2002), 5, 3-19 ("[P]roduct quality – but particularly a more favorable side effect profile – has a very substantial impact on product market share." p. 17); Charles King, "Marketing, Product Differentiation, and Competition in the Market for Antiulcer Drugs," HBS Working Paper 01-014 (2002).

This is also true in other economic markets. In the automobile industry, for example, recalls have been shown to lower the resale price of cars. *See* R. S. Hartman and M. Doane, "The Use of Hedonic Analysis for Certification and Damage Calculations in Class Action Complaints," *Journal of Law, Economics and Organization*, Vol. 3, No. 2, Fall 1987, pp. 351-372.

96. If the news is particularly bad, sales may fall sharply.[194] When serious and life-threatening risks are identified, the FDA may require that they be prominently displayed in a "black box" warning.[195] The FDA recently recommended one for the popular pain killer Vioxx® because it increased the risk of heart attack and stroke in patients who took it for more than 18 months.[196] Often drugs receiving "black box" warnings, such as Vioxx, are withdrawn from the market entirely.[197]

97. Thus Warner-Lambert's and Pfizer's suppression of adverse information about Neurontin would have increased Neurontin off-label sales.

IX. Conclusions

[194] The scientific literature demonstrates the addition of a "black box" warning for a prescription drug can profoundly affect its sales. "For example, during the year after [the] FDA required a black box warning for Seldane® (terfenadine),[194] … the product's 'sales dropped from around $700 million to $450 million.'" Beach, *op. cit.*, p. 409 (footnotes omitted). Seldane was originally approved for the relief of symptoms associated with seasonal allergic rhinitis such as sneezing, rhinorrhea, pruritus, and lacrimation. Seldane was removed from the market in 1998. (http://www.rxlist.com/cgi/generic/terfen.htm). "After the FDA "black box" warning, the sales of droperidol decreased by 10-fold during 2002 compared with 2001." Ashraf S. Habib, and Tong J. Gan, "Food and Drug Administration Black Box Warning on the Perioperative Use of Droperidol: A Review of the Cases", *Anesth Analg*, Vol. 96, 2003, 1377–9.

[195] J.E. Beach et al., "Black Box Warnings in Rx Drug Labeling: Results of a Survey of 206 Drugs," *Food and Drug Law Journal*, Vol. 53 (1998), p. 403.

[196] Jennifer Corbett Dooren, "FDA Panel Recommends Limited Vioxx Return to U.S. Market," *Wall Street Journal*, 2/18/2005, available online at http://www.wsj.com.

[197] "Sixteen drugs … approved between 1975 and 2000 were withdrawn from the market between 1975 and 2000; 5 had acquired a black box warning prior to withdrawal." K.E. Lasser, P.D. Allen, S. Woolhandler, D.U. Himmelstein, S.M. Wolfe and D.H. Bor, "Timing of New Black Box Warnings and Withdrawals for Prescription Medications," *Journal of the American Medical Association*, Vol. 287, No. 17 (May 1, 2002), p. 2216.

98. The goal of pharmaceutical marketing is to influence the prescribing habits of physicians and increase drug sales. Marketing by pharmaceutical companies seeks to influence the prescribing patterns of doctors both directly and indirectly. To obtain information about drugs, physicians rely upon "opinion leader" physicians and colleagues, medical and scientific journal articles, experiences of other medical professionals, medical liaisons, pharmaceutical sales representatives and continuing medical education.

99. Pharmaceuticals firms interact directly with physicians primarily through their sales force representatives, who visit doctors in their offices and provide information about their drugs, often leaving free samples behind. Other channels of direct communication to physicians include direct mail and medical journal advertising.

100. Drug companies also influence physicians indirectly through influencing those who influence physicians in their decisions about which drugs to prescribe. Indirect channels of influence include self-influence through research, peer influence, colleagues, key opinion leaders and continuing medical education. Continuing medical education consists of educational activities that serve to maintain, develop, or increase the knowledge, skills, and professional performance of physicians and often take place in conferences, meetings, and events funded by pharmaceutical companies.

101. Many of marketing's effects are subtle and pervasive. Doctors are often unable to explain where they first learned about a drug. Although physicians frequently claim that they are immune to the marketing and the blandishments of pharmaceutical companies, studies have shown that doctors and their prescribing habits are influenced by pharmaceutical companies' marketing efforts.

102. In the case of Neurontin, activities that should have been independent of promotional intent were used to promote Neurontin. These included the use of continuing medical education, medical research, payment for published articles, and medical liaisons as well as the suppression of unfavorable study results. By blurring the distinction between medical and scientific activities and commercial and promotional activities, Warner-Lambert and allegedly Pfizer subverted the integrity of the scientific process for determining the efficacy and appropriateness of Neurontin for treating certain diseases but succeeded in dramatically increasing off-label prescriptions of Neurontin.

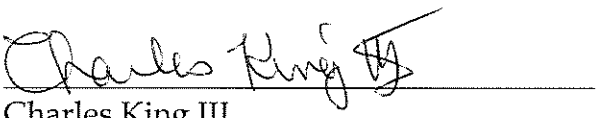
103. Based on my review of materials in this matter, I have reached the following conclusions:

a. The marketing and promotional efforts of Warner-Lambert and Pfizer were significant contributing factors to the off-label sales of Neurontin.

b. Off-label sales of Neurontin would have continued had Pfizer ceased off-label promotional activities for Neurontin.

c. The suppression of information about serious adverse events enabled growth in off-label sales.

d. Pfizer's off-label marketing of Neurontin indirectly influenced all, or substantially, all physicians prescribing of Neurontin.



Charles King III
October 22, 2007

Attachment A

CHARLES KING III

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EDUCATION

Ph.D. (Economics), Massachusetts Institute of Technology, 1997. Dissertation: *Empirical Studies of Marketing, Product Differentiation, Pricing and Competition.* Thesis advisors: Prof. Ernst R. Berndt and Prof. Glenn Ellison.

J.D., Yale Law School, 1979.

A.B. (*magna cum laude*), Harvard College, 1974.

EMPLOYMENT

2003 – *present*	Special Consultant, Greylock McKinnon Associates.
1997 – 2003	Assistant Professor, Harvard Business School.
1992 – 1997	Graduate Student, Research Assistant and Teaching Fellow, MIT.
1981 – *present*	President, Pleiades Consulting Group, Inc.
1988 – 1989	President, InterNos, Incorporated.
1987 – 1989	Manager, The Nelson Companies.
1985 – 1987	Vice President, Aox Incorporated.
1984 – 1985	President, ICM Technology Talent, Inc.
1981 – 1983	President, Xerxes Corporation.
1979 – 1981	Corporate Attorney, Ropes & Gray.

RESEARCH

Published Papers

Fleming, Lee, Charles King and Adam Juda (forthcoming). "Small Worlds and Regional Innovation," *Organization Science*.

Conley, Carey Thomson, Laurie B. Fisher, Jonathan P. Winickoff, Graham A. Colditz, Carlos A. Camargo, Jr., Charles King and Lindsay Frazier (2004). "State Tobacco Excise Taxes and Adolescent Smoking Behaviors in the United States," *Journal of Public Health Management Practice*, 10(6), 490-496.

King, Charles, Alvin J. Silk, and Niels Ketelhöhn (2003). "Knowledge Spillovers and Growth in the Disagglomeration of the U.S. Advertising Agency Industry," *Journal of Economics & Management Strategy*, 12(3), Fall 2003: 327-362.

King, Charles, and Michael Siegel (2001). "The Master Settlement Agreement with the Tobacco Industry and Cigarette Advertising in Magazines," *New England Journal of Medicine*, 345(7):504-511. In condensed form in "Statistics in the News: Chapter 13 Hypothesis Testing: The Classical Technique – Tobacco Advertising Targeting Youth," *Statistics for Business and Economics*, by Heinz Kohler, South-Western, 2003. (http://www.swlearning.com/quant/kohler/stat/resources/stats/ch13.html)

Cutler, David M., Arnold M. Epstein, Richard G. Frank, Raymond S. Hartman, Charles King, Joseph P. Newhouse, Elizabeth Richardson, and Meredith B. Rosenthal (2000). "How Good a Deal was the Tobacco Settlement? Assessing Payments to Massachusetts," *Journal of Risk and Uncertainty*, 21(2/3):235-261.

King, Charles, Michael Siegel, and Linda G. Pucci (2000). "Exposure of Black Youths to Cigarette Advertising in Magazines," *Tobacco Control*, 9(1):64-70.

King, Charles, and Michael Siegel (1999). "Brand-Specific Advertising in Magazines in Relation to Youth and Young Adult Readership, 1986-1994," *Nicotine & Tobacco Research* (1999) 1:331-340.

King, Charles, Michael Siegel, Carolyn Celebucki, and Greg N. Connolly (1998). "Adolescent Exposure to Cigarette Advertising in Magazines: An Evaluation of Brand-Specific Advertising in Relation to Youth Readership," *Journal of the American Medical Association* 279:516-520 (February 18, 1998).

King, Charles (1978). "Exceptions to Liability Under Section 16(b): A Systematic Approach," 87 *Yale Law Journal* 1430. Section 16(b) is the insider trading statute.

Published Papers (*continued*)

Peterson, Floyd W., and Charles King (1975), "A Model for Simultaneous Synchrotron and Inverse Compton Fluxes," *The Astrophysical Journal*, 195, 753. Models quasars and their energy requirements.

Working Papers

Gandal, Neil, Charles King and Marshall van Alstyne (2007), "Information Technology Use and Productivity at the Individual Level".

King, Charles (2002). "Marketing, Product Differentiation, and Competition in the Market for Antiulcer Drugs," HBS Working Paper 01-014.

King, Charles (2001). "Estimating the Elasticity of Demand and Cross-Border Effect for Cigarette Consumption in the New England States".

Work in Progress

Silk, Alvin J. and Charles King, *The Evolution of Advertising Agency Concentration.*

Published Cases

King, Charles and Das Narayandas, *Coca-Cola's New Vending Machine (A): Pricing To Capture Value, or Not? (9-500-068)*, Harvard Business School. *HBS Best Seller*.

Berndt, Ernst R., Charles King, Lisa Klein, and Alvin J. Silk, *Pepcid AC: The Race to Enter the OTC Market (9-500-073)*, Harvard Business School. Also published in *Problems and Cases in Health Care Marketing*, edited by John T. Gourville, John A. Quelch and V. Kasturi Rangan. McGraw-Hill Irwin, 2003.

EXPERT TESTIMONY

King, Charles (2007). *Abbott Laboratories v. Teva Pharmaceuticals Usa, Inc.*, United States District Court for the Northern District Of Illinois. Abbott Laboratories sought injunctive relief from generic competition from Teva.

King, Charles (2006, 2007). *Pennsylvania Employees Benefit Trust Fund v. Abbott Laboratories et al.*, United States District Court for the District of Delaware. Defendants allegedly maintained and extended their monopoly power by repeatedly changing the form and strength of their cholesterol lowering drug TriCor® to delay or preclude other manufacturers from bringing generic versions of the drug to market.

King, Charles (2005). "Marketing Zantac in Canada," *GlaxoSmithKline, Inc. v. Her Majesty the Queen*, Tax Court of Canada. The Canada Revenue Agency challenged the transfer price for ranitidine paid by Glaxo Canada to a non-resident, non arm's-length supplier for the taxation years 1990 to 1993.

King, Charles (2005). *Leoda Anderson v. Merck & Co., Inc.*, Superior Court of the State of California for the County of Los Angeles. Defendants allegedly fraudulently failed to disclose the serious cardiovascular risks associated with Vioxx® and/or that Vioxx® is no more effective than traditional non-steroidal anti-inflammatory drugs.

King, Charles (2004). *Stop & Shop Supermarket Co. et al. v. SmithKline Beecham Corp.*, United States District Court for the District of Eastern Pennsylvania. Defendants allegedly excluded competition in the market for the popular antidepressant Paxil® and its generic equivalents through sham litigation and fraudulent patent applications.

King, Charles (2003). *In Re Relafen Antitrust Litigation*, United States District Court for the District of Massachusetts. Defendants allegedly violated antitrust laws by extending and abusing their monopoly power through sham patent litigation against generic manufacturers to delay the introduction of generic versions of Relafen®, a drug used to treat arthritis.

King, Charles (2003). *Heindel et al. v. Pfizer et al.*, United States District Court for the District of New Jersey. Defendants allegedly advertised and marketed Celebrex® and Vioxx® as providing safe and effective pain relief without disclosing their health risks, which may include serious cardiovascular problems.

King, Charles (2002). "The Effect of the Master Settlement Agreement on the Exposure of Young People to Tobacco Marketing," Testimony Before the Senate Committee on Governmental Affairs Subcommittee on Oversight of Government Management, Restructuring, and the District of Columbia, United States Senate, May 14, 2002. (http://govt-aff.senate.gov/051302king.pdf)

EXPERT TESTIMONY (continued)

King, Charles (2001). "Youth Exposure and Targeting by Cigarette Companies," *Daniels v. Philip Morris et al*., Superior Court of the State of California for the County of San Diego.

Cutler, David M., Arnold M. Epstein, Richard G. Frank, Raymond S. Hartman, Charles King, Joseph P. Newhouse (1998). "The Impact of Smoking on Medicaid Spending in Massachusetts: 1970-1998 – Report on Methods, June 15, 1998," *The Commonwealth of Massachusetts v. Philip Morris, et. al.*, Superior Court for the Commonwealth of Massachusetts for the County of Middlesex.

Cutler, David M., Arnold M. Epstein, Richard G. Frank, Raymond S. Hartman, Charles King, Joseph P. Newhouse (1998). "The Impact of Smoking on Medicaid Spending in Massachusetts: 1970-1998 – Results from the Inclusive Approach for Adults, July 1, 1998," *The Commonwealth of Massachusetts v. Philip Morris, et. al.*, Superior Court for the Commonwealth of Massachusetts for the County of Middlesex.

Cutler, David M., Arnold M. Epstein, Richard G. Frank, Raymond S. Hartman, Charles King, Joseph P. Newhouse (1998). "The Impact of Smoking on Medicaid Spending in Massachusetts: 1970-1998 – Results for the Disease-Specific Approach for Adults and Overall Summary, July 11, 1998," *The Commonwealth of Massachusetts v. Philip Morris, et. al*,. Superior Court for the Commonwealth of Massachusetts for the County of Middlesex.

TEACHING

New Course Development

Harvard Business School, Ph.D. Program, Boston, Massachusetts.

Information and Network Economics, First year Ph.D. course. Spring 2001, 2002 and 2003.

Management and Markets: Organizational Economics and Strategy, First year Ph.D. course. Spring 2002 and 2003.

Additional Teaching Experience

Harvard Business School, Boston, Massachusetts.

First Year Marketing, MBA Course, Fall 1997, 1998; Spring 2000.

Doctoral Marketing, Ph.D. Course, Summer 1998.

Merck Harvard Executive Business Program, Spring 1998.

IBM Premier Program, Faculty Group, Cambridge, Massachusetts.

Competition and Strategy, 1998 – 2003.

Massachusetts Institute of Technology, Cambridge, Massachusetts, Teaching Assistantships.

14.30: Introduction to Statistical Methods in Economics, Spring 1997. (Prof. Jushan Bai)

14.01: Principles of Microeconomics, Fall 1994. (Prof. Franklin Fisher)

Dartmouth College, Hanover, New Hampshire. Visiting Assistant Professor.

Environmental Law and Policy Seminar, 1982. (with Prof. Douglas Ryan)

AWARDS AND FELLOWSHIPS

Best Reviewer Award, *Journal of Public Policy and Marketing*, 2003.
Faculty Research Fellow, National Bureau of Economic Research 2003-2004.
IBM Premier Executive Education Program, 2003.
Massachusetts Department of Public Health Grant, 1997.
Industrial Performance Center Doctoral Fellowship, 1995.
SHSS Tuition Fellowship Awards, 1993, 1994.
World Economy Laboratory Summer Fellowships, 1993, 1994.
Olin Foundation Fellowship, 1992.
Sigma Xi, Scientific Research Society of North America, 1974.
Harvard College Scholarship, 1972, 1973.
John Harvard Scholarship, 1971.
National Merit Finalist, 1970.
Bausch & Lomb Science Award, 1970.
Scientific American First Prize, 1970.

PROFESSIONAL ACTIVITIES

Editorial & Professional Service

President and Board Member, *Yale Law Journal Corp.*, 2007.

Alumni Advisory Board Member, *Yale Law Journal*, 2004-2007.

Program Reviewer, *The Robert Wood Johnson Foundation*, Substance Abuse Research Program. 2002 - present.

Editorial Review Board Member, *Journal of Public Policy & Marketing*. 2001 - present.

Member, *Harvard Tobacco Control Working Group*. 1998 - present.

Ad Hoc Referee

American Economic Review
Journal of Economics and Management Strategy
Journal of Health Economics
Journal of Industrial Economics
Journal of Public Policy & Marketing
Robert Wood Johnson Foundation
Tobacco Control

Thesis Committee

Niels Ketelhöhn, Ph.D., Harvard Business School (Competition and Strategy 2003).

Professional Affiliations

American Association for the Advancement of Science
American Astronomical Society
American Economics Association
American Marketing Association

Attachment B

Attachment B: Documents Relied Upon

Legal Documents

Boris, John, Deposition, *United States v. Pfizer Inc. and Parke-Davis*, Case No. 96-11651-PBS, September 16, 2002.

Information, *United States of America v. Warner-Lambert Company LLC*, United States District Court, District of Massachusetts, May 13, 2004.

Knoop, John M., Deposition, *United States v. Pfizer Inc., and Parke-Davis*, Case No. 96-11651-PBS, September 25, 2002.

Landefeld, C. Seth and Michael Steinman, Affidavit of C. Seth Landefeld, M.D., and Michael Steinman, M.D., *United States of America ex rel. David Franklin v. Pfizer, Inc., and Parke-Davis, Division of Warner-Lambert Company*, United States District Court for the District of Massachusetts, Civil Action No. 96-11651-PBS, May 19, 2003.

Marino, John, Deposition, *In re Neurontin Marketing Sales Practices, and Products Liability Litigation*, Master File No. 04-10981, MDL Docket No. 1629, July 2, 2007 and July 3, 2007.

Parker, James, Deposition, *United States v. Pfizer Inc., and Parke-Davis*, Case No. 96-11651-PBS, May 17, 2002.

Sentencing Memorandum of the United States, *United States of America v. Warner-Lambert Company LLC*, United States District Court for the District of Massachusetts, Criminal No. 04-10150 RGS, June 2, 2004.

Bates Documents

0008597-608

Pfizer APande 0000544-48

Pfizer_AFannon_0002912-67

Pfizer_AFannon_0002934

Pfizer_CGrogan_0005992-6002

Pfizer_CTaylor_0000414

Pfizer_JMarino_0000153-7

Pfizer_JMarino_0000363-7

Pfizer_JMarino_0000703-4

Pfizer_JMarino_0000809

Pfizer_LeslieTive_0020985-6

Pfizer_JMarino_0001272

Pfizer_LAlphs_0084359-479

Pfizer_LCastro_0002678-82

Pfizer_LCastro_0074739-40

Pfizer_LeslieTive_0020985-6

Pfizer_LeslieTive_0080783-4

Pfizer_LKnapp_0009569-73

Pfizer_LKnapp_0070537-44

Pfizer_LKnapp_0070556-8

Pfizer_LKnapp_0091179-82

Pfizer_LTive_0006484-97

Pfizer_LTive_0008259

Pfizer_LTive_0008275-92

Pfizer_LTive_0008284

Pfizer_LTive_0009300-27

Pfizer_RGlanzman_00000677

Pfizer_RGlanzman_0000669

Pfizer_RGlanzman_0054596-609

Pfizer_RGlanzman_0134501-3

Pfizer_SDoft_0026340

Pfizer_SDoft_0026346

Pfizer_SDoft_0026347-49

Pfizer_SDoft_0026365

V 082736 – 082761

V042352-63

V047116-29

V049269-V049274

V053848-77

V057651-92

V058083-95

V069673-6

V082736-61

V084073

V086787-92

V090268

V090836-77

V091389

W003095-109

WL 07520-47

WLC_CBU_038946

WLC_FRANKLIN_0000038501-02

X001884-900

X003630-58

X005102-X005110

X005384-86

X005926-50

X028920-24

X028957-62

X028965-69

X028974-75

X029017-25

X029226-7

Other Documents

21 CFR 202.1.

Adams, M., "Drug reps use psychological tactics to successfully influence doctors' prescribing habits", *News Target Network*, July 30, 2007, http://www.newstarget.com/021956.html, accessed September 21, 2007.

American Economic Association, Papers and Proceedings of the 107th Annual Meeting of the American Economic Association, Washington D.C.

Angell, Marcia, *The Truth About the Drug Companies How They Deceive Us and What to do about it*, Random House Press, 2004.

Arrow, K., "Uncertainty and the Welfare economics of medical care," *The American Economic Review*, 53:941-73, 1963.

Avorn, J., M. Chen, and R. Hartley, "Scientific Versus Commercial Sources of Influence on the Prescribing Behavior of Physicians," *American Journal of Medicine,* 73 (1), 4–8, 1982.

Azoulay, P., "Do Pharmaceutical Sales Respond to Scientific Evidence?" *Journal of Economics & Management Strategy*, Volume 11, No. 4, Winter 2002, pp. 551-594.

Beach, J.E., et al., "Black Box Warnings in Rx Drug Labeling: Results of a Survey of 206 Drugs," *Food and Drug Law Journal*, Vol. 53 (1998), p. 403.

Benedetti, Fabrizio and Martina Amanzio, "The Neurobiology of Placebo Analgesia: From Endogenous Opiods to Cholecystokinin," *Progress in Neurology*, Vol. 51, pp. 109-125, 1997.

Berndt, E.R., A. Bhattacharja, D.N. Mishol, A. Arcelus and T. Lasky, "An Analysis of the Diffusion of New Antidepressants: Variety, Quality, and Marketing Efforts," *Journal of Mental Health Policy and Economics* (2002), 5, 3-19

Berndt, E.R., C. King, L. Klein and A.J. Silk, "Pepcid AC: The Race to Enter the OTC Market," (9-500-073), Harvard Business School.

Berndt, Ernst R., Linda Bui, David R. Reiley and Glen Urban, "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," *American Economic Review* (1995), 85, 2, 100-105.

Berndt, Pindyck and Azoulay, "Consumption Externalities and Effusion in Pharmaceutical Markets: Antiulcer Drugs," The Journal of Industrial Economics, June 2003, 243-270.

Bowman, M., and D. Pearle, "Changes in Drug Prescribing Patterns Related to Commercial Company Funding of Continuing Medical Education," *Journal of Continuing Education in the Health Professions* 8:13–20, 1988.

Calfee, J. E., and D. J. Ringold (1994), "The 70% Majority: Enduring Consumer Beliefs about Advertising," Journal of Public Policy and Marketing, Volume 13, Pp. 228-28.

Chren, M., and C. Landefeld, "Physicians' Behavior and Their Interactions with Drug Companies: A Controlled Study of Physicians Who Requested Additions to a Hospital Drug Formulary," *The Journal of the American Medical Association*, 271, 684-689, 1994.

Christiansen, Dale D., and Albert J. Wertheimer (1979), "Sources of Information and Influence upon New Drug Prescribing among Physicians in an HMO," Soc. Sci. & Med., pages 313-322.

Clayton, E., "Tis Always the Season for Giving," CALPIRG Report, September 2004; Editorial Staff, "Pharmaceutical Marketing to Physicians: Free Gifts Carry a High Price," *American Medical News*, 10 June 2002.

Cutler, D., A. Epstein, R. Frank, R. Hartman, C. King, J. Newhouse, E. Richardson and M. Rosenthal, "How Good a Deal was the Tobacco Settlement?: Assessing Payments to Massachusetts," *Journal of Risk and Uncertainty* (2000), 21 (2/3).

Davidoff, F., C.D. DeAngelis, J.M. Drazen, M.G. Nicholls, J. Hoey, L. Hojgaard, *et al*. "Sponsorship, Authorship, and Accountability," *The New England Journal of Medicine*, Volume 345(11), September 2001, 825-82.

Davidoff, F., C.D. DeAngelis, J.M. Drazen, M.G. Nicholls, J. Hoey, L. Hojgaard, *et al*. "Sponsorship, Authorship, and Accountability," *The Journal of the American Medical Association*, Volume 286(10), September 2001, 1232-1234.

Dogramatzis, D., *Pharmaceutical Marketing: A Practical Guide*, Colorado: IHS Health Group, 2002.

Dooren, Jennifer Corbett, "FDA Panel Recommends Limited Vioxx Return to U.S. Market," *Wall Street Journal*, 2/18/2005, available at http://www.wsj.com.

Drugs.com website, http://www.drugs.com/top200_2003.html, accessed October 22, 2007.

Families USA Foundation, "Off the Charts: Pay, Profits and Spending by Drug Companies," Families USA Publication No. 01-104, July 2001, p. 1.

Gonul, F., F. Carter, E. Petrova and K. Srinivasan, "Promotion of Prescription Drugs and Its Impact on Physician Choice Behavior," Journal of Marketing, 65:3, pp. 79-90, 2001.

Grimshaw, J. M., et al., "Changing physicians' behavior: What works and thoughts on getting more things to work", *Journal of Continuing Education in the Health Professions*, Vol. 22, 2002, pp.237-43.

Habib, Ashraf S., and Tong J. Gan, "Food and Drug Administration Black Box Warning on the Perioperative Use of Droperidol: A Review of the Cases", *Anesth Analg*, Vol. 96, 2003, 1377–9.

Hamer et al., "Gabapentin use in a managed medicaid population", *Journal of Managed Care Pharmacy*, Vol. 8, No. 4, 2002, pp. 266-71.

Harikresh Nair, Puneet Manchanda, Tulidaa Bhatia, "Asymmetric Peer Effects in Physician Prescription Behavior: The Role of Opinion Leaders."

Hartman, R. S., and M. Doane, "The Use of Hedonic Analysis for Certification and Damage Calculations in Class Action Complaints," *Journal of Law, Economics and Organization*, Vol. 3, No. 2, Fall 1987, pp. 351-372.

Haug, James, "Physicians' preferences for information sources: a meta-analytic study", *Bull Medical Library Association*, Vol.85, July 1997.

Hemminki, E., (1997), "Content Analysis of Drug-Detailing by Pharmaceutical Representatives," Med Educ 11:210-215.

Hodges, B., "Interactions with the Pharmaceutical Industry: Experiences and Attitudes of Psychiatry Residents, Interns and Clerks," *Canadian Medical Association Journal,* 1:153(5):553-9, September 1995.

Hovland, C. I., and W. Weiss (1951), "The Influence of Source Credibility on Communication Effectiveness," Public Opinion Quarterly, Volume 15, Pp. 635-650.

Hrobjartsson, Asbjorn and Peter Gotzche, "Is the Placebo Powerless? An Analysis of Clinical Trials Comparing Placebo with No Treatment," *The New England Journal of Medicine*, Vol. 344, No. 21, May 24, 2001.

Hurwitz, M.A., and R.E. Caves, "Persuasion or Information? Promotion and the Shares of Brand Name and Generic Pharmaceuticals," *Journal of Law and Economics*, Vol. 31(2), Oct. 1988, p. 302.

King, C., and D. Narayandas, "Coca-Cola's New Vending Machine (A): Pricing To Capture Value, or Not?" (9-500-068), Harvard Business School

King, C., III, "Marketing, Product Differentiation and Competition in the Market for Antiulcer Drugs," Boston MA: Harvard Business School Working Paper No. 01-014, 2000 (http://papers.ssrn.com/sol3/papers.cfm?abstract_id=891128);

King, C., Statement Before the Committee on Governmental Affairs, Subcommittee on Oversight of Government Management, Restructuring and the District of Columbia, United States Senate, May 14, 2002 (available at <http://hsgac.senate.gov/051302king.pdf> as accessed October 2007).

Lasser, K.E., P.D. Allen, S. Woolhandler, D.U. Himmelstein, S.M. Wolfe and D.H. Bor, "Timing of New Black Box Warnings and Withdrawals for Prescription Medications," *Journal of the American Medical Association*, Vol. 287(17), May 1, 2002, p. 2216.

Leffler, K., "Persuasion or Information? The Economics of Prescription Drug Advertising," *The Journal of Law and Economics*, Vol. 24, April 1981, pp. 45-74.

Lewis, D.A., R. Michels, D.S. Pine, S.K. Schultz, C.A. Tamminga, R. Freedman, "Conflict of Interest," *The American Journal of Psychiatry*, Volume 163(4), April 2006, 571-3.

Lexchin, J., (1997), "What Information to Physicians Receive from Pharmaceutical Representatives?" Can Fam Physician 43: 941-945.

Manchanda, P., and P. Chintagunta, "Responsiveness of Physician Prescription Behavior to Salesforce Effort: An Individual Level Analysis", *Marketing Letters*, Vol. 15, July 2004, pp. 129-45.

Mayo Clinic website, http://www.mayoclinic.com/health/postherpetic-neuralgia/DS00277, accessed October 22, 2007.

MediceNet.com website, "Definition of Placebo Effect," http://www.medterms.com/script/main/art.asp?articlekey=31481, accessed October 22, 2007.

Molloy, W., D. Strand, G. Guyatt et al. (2002), "Assessing the Quality of Drug Detailing," Journal of Clinical Epidemiology 55:825-832.

Newhouse, J.P., and the Insurance Experiment Group, *Free for All? Lessons from the RAND Health Insurance Experiment*, Cambridge: Harvard University Press, 1993.

Pande, A.C., J.G. Crockatt, C.A. Janney, J.L. Werth, G. Tsaroucha, "Gabapentin in bipolar disorder: a placebo-controlled trial of adjunctive therapy," Gabapentin Bipolar Disorder Study Group. *Bipolar Disord*. 2000, 2: 249-55.

Pande, Atul, Statement of Atul Pande, M.D., F.R.C.P.C., "Combination Treatment in Bipolar Disorder," Third International Conference On Bipolar Disorder, June 18, 1999.

Peay, M.Y., and E.R. Peay, "The Role of Commercial Sources in the Adoption of a New Drug," *Social Science & Medicine*., 26:1183-1189, 1988.

"Performance of Sales Representatives in France: Still Bad," Prescrire International 2003, 12: 153-1 54.

Peterson, Melody, "Suit Says Company Promoted Drug in Exam Rooms," New York Times, May 15, 2002, C1.

Piercy, Marlena A., John J. Sramek, Neal M. Kurtz and Neal R. Cutler, "Placebo Response in Anxiety Disorders," *The Annals of Pharmacotherapy*, Vol. 30, No. 9, 1996, pp. 1013-1019.

Prakash, Snigdha, NPR, "The Selling of Neurontin," January 16, 2003, available at http://www.npr.org/templates/story/story.php?storyId=920362.

Quitkin, Frederic M., "Placebos, Drug Effects, and Study Design: A Clinician's Guide," *American Journal of Psychiatry*, 156:6, June 1999.

Radley, D.C., S. N. Finkelstien and S. Stafford, "Off-label Prescribing Among Office-Based Physicians", *Arch Intern Med.* , Vol. 166, May 8, 2006, pp. 1021-1026.

Rizzo, J., "Advertising and Competition in the Ethical Pharmaceutical Industry: The Case of Antihypertensive Drugs," Journal of Law and Economics, 42:1, pp. 89-116, 1999.

Roughead, E.E., A. L. Gilbert and K.J. Harvey (1998), "Self-Regulatory Codes of Conduct: Are They Effective in Controlling Pharmaceutical Representatives' Presentations to General Medical Practitioners?" Int J Health Serv 28:269-279.

Rx List website, "Seldane," http://www.rxlist.com/cgi/generic/terfen.htm, accessed October 22, 2007.

Sandberg, W., et al., "The Effect of Educational Gifts from Pharmaceutical Firms on Medical Students' Recall of Company Names or Products," *Academic Medicine*, 72:916-918, 1997.

Scherer, F.M., "The Pharmaceutical Industry" in eds. A.J. Culyer and J.P. Newhouse, *Handbook of Health Economics*, Elsevier, 2000, pp. 1300-1302.

Scherer, F.M., and D. Ross, *Industrial Market Structure and Economic Performance*, Third Edition, Boston: Houghton Mifflin Company, 1990, p. 573.

Schweitzer, S., *Pharmaceutical Economics and Policy*, New York: Oxford University Press, 1997, p. 43. From E.R. Berndt, "The U.S. Pharmaceutical Industry: Why a Major Growth in Times of Cost Containment?" *Health Affairs*, Vol. 20(2) 2001, pp. 111-2:

Shaughnessy, A. E. , D. C. Slawson and J.H. Bennett (1994), "Separating the Wheat from the Chaff: Identifying Fallacies in Pharmaceutical Promotion," J Gen Intern Med 9: 563-568.

Steinman et al., "The Promotion of Gabapentin: An Analysis of Internal Industry Documents," Annals of Internal Medicine, August 16, 2006, 145 (4).

Steinman, Michael A., G. Michael Harper, et al. (2007), "Characteristics and Impact of Drug Detailing for Gabapentin," PLoS Medicine, April 2007, volume 4, issue 4, e134, pp. 0743–0751.

Stryer, D., and L.A. Bero, "Characteristics of Materials Distributed by Drug Companies. An Evaluation of Appropriateness," J. Gen Intern Med 11: 575-583.

Sutton, J., *Technology and Market Structure*, Cambridge: The MIT Press, 1998.

US Department of Justice, "Warner-Lambert to Pay $430 Million to Resolve Criminal & Civil Health Care Liability Relating to Off-Label Promotion," available at http://www.usdoj.gov/opa/pr/2004/May/04_civ_322.htm, accessed October 14, 2007.

Waxman, H.A., (2005), "Memorandum to Democratic Members of House Government Reform Committee: a Marketing of Vioxx to Physicians," available: HTTP://www.democrats.reform.house.gov/documents/20050505114932-41272.pdf.

Wazana, A., "Physicians and the Pharmaceutical Industry," *The Journal of the American Medical Association,* 283:373-380, 2000; A. Fugh-Berman, "The Corporate Coauthor," *Journal of General Internal Medicine,* 20(6):546-8, Jun 2005.

Ziegler, M. G., P. Lew, B. C. Singer (1995) "The Accuracy of Drug Information from Star Pharmaceutical Sales Representatives," JAMA 273: 1296-1298.

Attachment C

Attachment C

The 2000 Neurontin Program Summary, shown in Table 1 below, clearly illustrates that Pfizer had more medical education programs directed towards off-label uses of Neurontin. The only approved use of Neurontin in 2000 was for adjunctive treatment of epilepsy, yet only 19 of the 764 medical education program events, or 2.5% of total events, in 2000 were for epilepsy.

Table 1:

Neurontin Program Summary – 2000				
	Unique Programs	Events	Physicians	Physicians per Event
Promotional Programs	896	1,074	22,070	20
Medical Education Programs	41	764	37,600	
Epilepsy	16	19	7,700	82
Pain	17	651	28,400	44
Psychiatry	8	94	1,500	77

Recreated from "Neurontin 2001 U.S. Operating Plan", Pfizer_RGlanzman_0000650-0000776, at Pfizer_RGlanzman_0000727.

Table 2 shows the events for 2000, taken from a draft version of the Neurontin 2001 Situation Analysis, [1] and Figure 1 shows the medical education plan for 2001 from the Neurontin 2001 U.S. Operating Plan.[2] An interesting point of departure between the draft version of the Neurontin 2001 Situation Analysis and the final Neurontin 2001 U.S. Operating Plan is that in the draft, medical education directed toward off-label uses are identified as "Education Support in the Area of Emerging Uses", yet in the final version, medical education directed towards unapproved uses of Neurontin are incorporated into the same table as medical educational events for approved uses in epilepsy. Figure 1 lists many educational events for teaching doctors about off-label uses of Neurontin, such as the symposia entitled "Emerging Uses of AEDs in Psych".

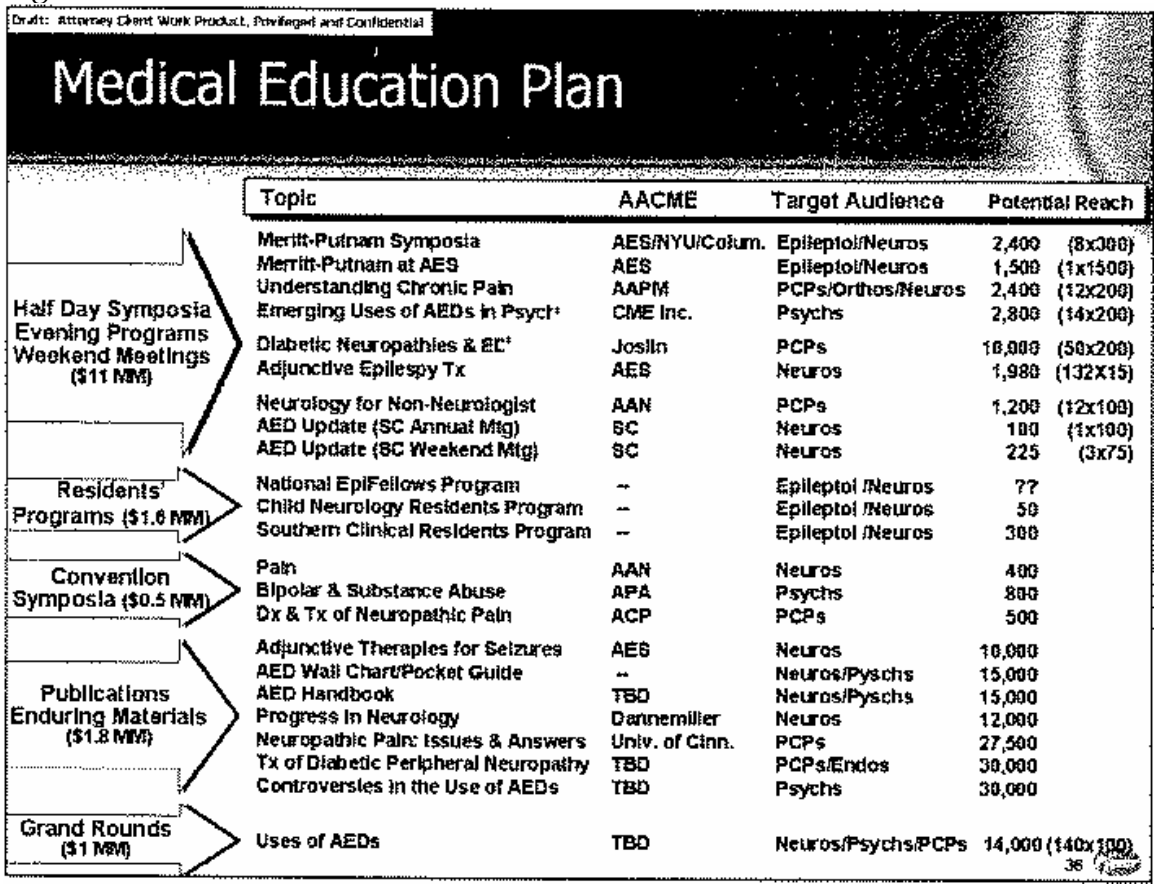
[1] "Neurontin 2001 Situation Analysis", Pfizer_JMarino_0002350-84.
[2] See "Neurontin 2001 U.S. Operating Plan", Pfizer_RGlanzman_0000650-0000776.

Table 2[3]: Education Support in the Area of Emerging Uses[4] in 2000

Event	Number	Average Attendance	Estimated Total Attendance
CME Pain Symposia entitled "New Treatment Options in Management of Pain: The Role of Anticonvulsants".	75 events	Average attendance per event was 100.	7,500 (75 events x 1,000 attendees/event)
CME dinner series entitled "Re-evaluating Neuropathic Pain Treatment Algorithms".	125 dinners	Average attendance per event was 30.	3,750 (125 dinners x 30 attendees/dinner)
CME Grand Rounds series entitled "Applications of Anticonvulsants in Neurological Conditions".	75 events	Not provided	N/A
CME dinner series entitled "Diabetic Neuropathies and Microvascular Complications".	37 dinners	Average attendance per event was 180.	6,660 (37 dinners x 180 attendees/dinner)
CME PCP pain symposia entitled 'Practical Approaches to the Treatment of Chronic Neuropathic Pain".	16 events	Not provided	N/A
CME Pain Satellite Symposia at American Academy of Neurology	1 symposia	Not provided	N/A
CME Pain Satellite Symposia at American Pain Society	1 symposia	Not provided	N/A
CME Pain Satellite Symposia at American Geriatric Society	1 symposia	Not provided	N/A
CME Pain Satellite Symposia at American Society of Addiction Medicine	1 symposia	Not provided	N/A
CME Pain Satellite Symposia at American Physicians Assistants Association	1 symposia	Not provided	N/A

[3] Created from "Continue publication/education support in the area of emerging uses" of Neurontin 2001 Situation Analysis (Pfizer_JMarino_0002350-84, at Pfizer_JMarino_0002375).
[4] According to John Marino, "emerging uses" are unapproved uses. Marino deposition, pp.119-120.

Figure 1:



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